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TPS 01
CLINICAL IMMUNOLOGY FROM AUTOIMMUNITY TO CANCER

TP0615 | The impact of serum anti-neutrophil cytoplasmic antibody (ANCA) on clinical presentation and outcome in pediatric onset systemic lupus erythematosus (SLE) patients

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by several immunological abnormalities. Antineutrophil cytoplasmic antibodies (ANCA) are autoantibodies against cytoplasmic antigens within neutrophils and monocytes. The presence of ANCA in SLE had been known for 20 years. However, it is association with disease activity including clinical features, histological and outcomes with the presence of ANCA in pediatric-onset SLE patients is very limited.

Method: We conducted a retrospective study of pediatric-onset SLE patients with ANCA data in a tertiary referral center over a 3-year-period (2015-2018). Clinical characteristics, laboratory data, histological features, treatment and outcome were recorded.

Results: A total of 70 children of pediatric-onset SLE patient were enrolled. Among these patients, 9 (13%) had ever positive in ANCA in follow-up. Median ages at diagnosis were 13.78 years and 12.67 years in the ANCA-positive and ANCA-negative group, respectively. 3 patients with elevation of C-ANCA level and 6 patients had increase P-ANCA level. Patients with positive finding in ANCA level have tendency to hematuria ($P = 0.026$) and initial presentation with anti-phospholipid ($P = 0.022$). Besides, no differences were observed in laboratory data and clinical conditions including fever, neurological presentation, pulmonary hemorrhage, arthralgia and skin involvement (all $P < 0.05$). Of the 51 SLE patients with renal biopsy (7 were seropositive in ANCA), there was no significant difference between renal histology between the groups.

Conclusion: The serum ANCA was detected in cases of lupus in current study. The presence of ANCA in pediatric-onset SLE patients has different clinical manifestation. Further investigation is warranted to clarify our findings and possible pathogenesis.

TP0616 | Comparison of different methods in detection of antimitochondrial antibodies and their diagnostic utility

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Background: Indirect immunofluorescence assay (IFA), liver immunoblot, and enzyme-linked immunosorbent assay (ELISA) have been using for the detection of antimitochondrial antibodies (AMA). The aim of our study is to compare these methods in view of their performances to detect AMA and their utility for clinical diagnosis.

Method: Retrospectively, between January 2015 and january 2016, 11004 seras with ANA-IFA (HEp2 cells) (IMMCO diagnostics), 3240 seras with LKM-IFA (Liver-kidney-microsomal) (EUROIMMUNE) and 1177 seras with liver immunoblot (EUROIMMUNE) were studied. First of all, we looked for positivity rates by LKM-IFA, than we focused on ANA and liver immunoblot results with their clinical diagnosis. Clinical data were obtained from hospital records. Ethical approval and written informed consent were obtained.

Results: 11004 seras analysed by ANA-IFA; 75 of them (0.06%) had AMA like cytoplasmic pattern. 3240 seras analysed by LKM-IFA, 111 (3.4%) had positive AMA pattern. 1177 seras analysed by liver immunoblot and 97 (8.2%) had AMA M2. Among 111 patients with AMA pattern, 84 (75%) had autoimmune hepatitis/primary biliary cirrhosis/ chronic liver diseases (OIH/PBS/CLD) (positive predictive value of LKM-IFA: 75%). 105 of 111 LKM-IFA positive patients were analysed by ANA, 97 of them showed typical cytoplasmic AMA pattern (92%) and in 4 atypical cytoplasmic (3.8%) pattern. Totally 101 of 105 (%96) ANA-IFA analyses are compatible with the results found by LKM-IFA. Among those 101 with AMA pattern detected by ANA-IFA, 80 (80%) had OIH/PBS/CLD (positive predictive value of ANA-IFA: 80%). 74 of 111 LKM-IFA positive patients were analysed by liver immunoblot, and 69 were AMA M2 positive (93%). Among those 69 AMA-M2 positive patients detected with liver immunoblot, 59 (85%) had OIH/PBS/CLD (positive predictive value of liver immunoblot: 85%).

Conclusion: Serum AMA positivity is the diagnostic hallmark of PBC/OIH/CLD, as they are detected in 90%-95% of affected individuals. In our study, among LKM-IFA positive patients; 75% had liver diseases; but also ANA-IFA and liver immunoblot detected the

80% - 85% of patients with liver diseases, respectively. Our results indicated a significant correlation between LKM-IFA and ANA-IFA. In conclusion, LKM-IFA remains the method of choice for screening assay, but immunoblot may be useful for confirmation and identification of AMA positivity.

TP0617 | Comparison of different methods in detection of Anti-DsDNA antibodies and their diagnostic utility

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Background: Anti-dsDNA is one of the primary autoantibodies present in patients with systemic lupus erythematosus (SLE). Enzyme-linked immunosorbent assay (ELISA), Crithidia luciliae immunofluorescence assay (CLIFT), and radioimmunoassay methods (FARR-RIA) are used to determine dsDNA antibodies. The aim of our study is to search the positivity rates of CLIFT and to determine the most efficient strategy to test anti-dsDNA for SLE diagnosis.

Method: This retrospective study analyzed 3242 seras which were sent to our laboratory between January 2015 and January 2016 for CLIFT. We compared the positive CLIFT (IMMCO Diagnostics) results with antinuclear antibody immunofluorescence (ANA-IFA, Hep2, IMMCO Diagnostics), ELISA (EUROIMMUNE) and ANA immunoblot (EUROIMMUNE) results. We searched for their clinical data from hospital records. Positive predictive value (PPV) and positive percentage of results were calculated. Hospital's ethics committee approval and written informed consent were obtained.

Results: Among 3242 seras, 72 (2.2%) samples, which were belong to 64 patients (seras from 9 patients were analysed twice), were positive for anti-dsDNA by CLIFT. Of those CLIFT positive patients, the diagnosis was SLE in 47 (73%) (PPV of CLIFT: 73%). Of those 64 patients, 61 patients were detected by ANA-IFA, and all were positive (%100). In 36 (59%), peripheral and homogenous patterns were detected. Among 36 patients with ANA patterns compatible with dsDNA; 30 (83%) had SLE (PPV of ANA: 83%). Forty six of 64 patients were analysed by ANA immunoblot, 30 were positive (65%) for dsDNA. Twenty two (73%) of 30 patients with positive dsDNA by ANA immunoblot had SLE (PPV of ANA immunoblot: 73%). Twenty five of 64 patients were analysed for dsDNA antibody by ELISA; 18 were found positive (72%); and 15 of them (83%) had SLE (PPV of ELISA: 83%).

Conclusion: CLIFT cannot substitute ELISA and ANA immunoblot, but can reduce their use, since the results of 3242 consecutive sera showed that only 2.2% of patients was tested positive for anti-dsDNA by CLIFT and needed quantitative confirmation by ELISA and immunoblot. CLIFT and ANA-IFA may be recommended for determination of dsDNA for first-line screening, and ANA immunoblot and ELISA for further confirmation and identification of dsDNA. For diagnosing SLE, as ANA-IFA has the high PPV for the first line screening; ELISA has the high PPV for the confirmation of diagnosis.

TP0619 | Evaluate the frequency of autologous serum skin test in patients with autoimmune diseases

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Background: The presence of functional autoantibodies against IgE receptors or against IgE bound to its receptor in cutaneous mast cells can be assessed *in vivo* using the autologous serum skin test (ASST). ASST is associated with several other autoantibodies in patients with chronic spontaneous urticaria (CSU). The aim of this study is to assess the positivity of ASST in patients with autoimmune diseases with or without chronic urticaria.

Method: This was a retrospective study of adult patients with autoimmune diseases (AID), excluding autoimmune thyroid disease, attended at a tertiary center. Patients who underwent ASST from 2005 to 2018 were included. Demographic data, the presence of associated chronic spontaneous urticaria (CSU), refractoriness of antihistamines, angioedema and frequency of autoantibodies were evaluated.

Results: Twenty-two patients with AID participated in the study, being 95.5% female. The mean age was 51.3 years, age at onset of AID was 38.8 years, and 50% of the patients had systemic lupus erythematosus (SLE). Sixteen patients had associated chronic urticaria, and of these, 12 (75%) presented CSU. ASST was positive in 68.2% of patients with AID. The anti-nuclear factor (ANF) was present in 77.3%, ranging from 1/80 to 1/1280. Antithyroid autoantibodies were distributed in positive anti-TPO in 27.3% and positive anti-TG in 36.4% of the patients. In patients with AID-associated CSU, urticaria preceded AID in 62.5% of them.

Conclusion: Our study observed a high frequency of positive ASST in patients with AID, regardless of the presence of associated chronic urticaria. Likewise, antithyroid autoantibodies were present in most AID patients, although autoimmune thyroid disease was excluded. Therefore, these results reinforce the association of several autoimmune diseases in the same patient, as described in the literature.

TP0620 | Therapeutic challenge regarding refractory idiopathic erythema nodosum—A case report

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Case report: Introduction: Erythema nodosum (EN) is a common form of panniculitis often found in female patients. There are important

identifiable triggers, such as sarcoidosis and inflammatory bowel disease. However, up to 50% of cases are considered idiopathic.

Case Description: A 47-year-old woman was sent to Internal Medicine consultation complaining of a 6-year history of persistent subcutaneous lesions suggestive of EN affecting her abdomen, arms and thighs, intermittent and symmetric bilateral inflammatory arthralgias of metacarpophalangeal joints and wrists. She denied constitutional symptoms, oral or genital ulcerations, xerophthalmia, xerostomia and Raynaud phenomenon. There was no history of drug allergy or recurrent infections. The previous investigation done at her hometown hospital showed a chronic disease anaemia with ANA positivity, an elevated ESR levels (80 mm/h), with a normal serum C3, C4, ACE and ASO levels. Tuberculosis was excluded, as well as HIV, HBV and HCV infection. A pathergy test, an endoscopic study and a thoracic CT-scan were performed, with no significant findings. Back then, she showed no therapeutic response to NSAIDS, potassium iodide, dapsone, azathioprine and 1 mg/kg daily of prednisone. At the time of our evaluation, she began combination therapy of steroids, methotrexate and hydroxychloroquine and was later hospitalized for further study. During admission, the serology for ANA and ENA antibodies came negative. She was also submitted to a full-body PET-CT-scan, which was normal. A cutaneous biopsy was performed, confirming EN. Considering the diagnosis of idiopathic and refractory EN (and despite all the therapeutic regimens that were tried), the patient remained symptomatic and started on biologic therapy with infliximab.

Conclusion: The majority of EN cases are self-limited and respond well to most immunomodulatory drugs. This case report highlights the rarity and severity of refractory idiopathic forms of EN as well as its defying management.

TP0621 | The strange case of an anti-neutrophil cytoplasmic antibody (ANCA) negative associated vasculitis

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Case report: Introduction: ANCA-negative vasculitis represents the fourth group of the revised Chapel-Hill classification, comprising an unusual seronegative and mixed pattern of granulomatosis with polyangiitis and microscopic polyangiitis.

Case Description: A 49-year-old woman was sent to Internal Medicine consultation complaining of a 8-month history of constitutional symptoms, oral ulcerations and low-grade fever. More recently, she referred general abdominal discomfort and self-limiting episodes of diarrhoea and urticaria affecting arms and legs. The diagnostic investigation started at her hometown hospital, showing chronic disease anaemia, elevated ESR levels, ANA positivity, ANCA negativity, normal serum ACE levels and excluding tuberculosis, as well as HIV, HBV, HCV and parasitologic infections. The GI tract endoscopic study found unspecific aphthoid erosions at the terminal ileum and ileal biopsies detected mild mucosal eosinophilic infiltration without granulomas. It was also noticed the presence of bilateral migratory and infracentimetric pulmonary nodular lesions, found in successive thoracic CT scans; bronchofibroscopy was inconclusive and endocarditis was excluded. She was hospitalized for further study. During admission, cryoglobulinemia, hypocomplementemia and hypergammaglobulinemia were excluded; the autoimmune serologic tests came again positive for ANA and negative for ANCA and anti-glomerular basal membrane antibodies. A full-body CT-scan was performed, showing an extensive area of confluent hypodense lesions located at the posterior and superior segments of the spleen, also detected in PET-CT scan. The histologic examination of splenic samples excluded lymphoma, but no other considerations were possible with available samples. It was assumed the diagnosis of ANCA-negative vasculitis and the patient began treatment with 1 mg/kg daily of prednisone and was discharged with progressively reduction dose of steroids in association with azathioprine. After 2 months of treatment, she noticed complete resolution of symptoms.

Conclusion: The pathogenic mechanisms underlying ANCA-negative vasculitis are still unknown. This is, to our knowledge, the first case of ANCA-negative vasculitis affecting lungs, spleen, skin and intestine.

TP0622 | Immunological characterization of Wilson disease

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Case report: Wilson disease (WD) is an inherited disorder of copper disposition in hepatocytes. Defective copper metabolism leads to hepatic copper retention and chronic liver injury. Other tissues (brain, eyes) may be damaged, due to copper toxicity. The pattern of inheritance is autosomal recessive. Mutations occur in the gene ATP7B encoding for the metal-transporting ATPase known as the WD-ATPase. The WD-ATPase is a multifunctional membrane-spanning protein which monitors hepatocellular levels of copper, contributes to the production of holoceruloplasmin and expedites biliary excretion of copper. WD-ATPase is also expressed in immune cells as well as lymphoid organs (spleen, lymph nodes). Only sporadic report exists on the immunological changes possibly occurring in patients affected by WD. Aim: the phenotypical and functional characterization of the immune system of a patient affected by WD, compared to healthy controls.

Methods: *Adaptive immune system:* Using flow cytometry, we assessed the following cell subsets in the isolated peripheral blood mononuclear cells: CD4 and CD8 T cells; Tregs; B cells; IgE+ B cells; gamma delta T cells; NK and NKT cells; basophils. Moreover, we monitored lymphocyte activation and proliferation response

towards Phytohaemoagglutinin-M. Finally, we evaluated total IgA/G/M/E levels.

Innate immune system: using RT-PCR we monitored the gene expression of 5-Lipoxygenase (5-LO), FLAP and Cysteinyl-leukotriene receptor (Cys-LTR), mainly expressed on innate immune cells. Finally the functional activity of 5-LO was assessed using HPLC technique.

Results: *Adaptive immune system:* we found an increase in total double negative T cells (DNT; $CD4^-/CD8^-$); gamma delta DNT cells, Tregs and NK cells. In contrast, CD4 and CD8 T cells were reduced. Interestingly, T cells had a basal activation and proliferation rate higher compared to the healthy control cells. The extent of the response towards PHA-M was also enhanced. No difference was observed in any of the Ig subclasses.

Innate immune system: No differences were observed in basophils, eosinophils and neutrophil count. However, in PMNL, the gene expression of 5-LO, FLAP and CysLTR is increased as well as the 5-LO functional activity.

Conclusions: WD probably induces a constant activation state of both adaptive and innate immune system that results in a re-shaping of the adaptive immune system. Moreover, the increase of gamma delta DNT cells suggests a chronic stimulation at the mucosal level.

TP0623 | IgG4 related disease and ligneous conjunctivitis in a girl: A coexistence or a relationship?

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Background: IgG4-related disease (IgG4-RD) is a systemic, fibroinflammatory disease with various presentations. It can involve any organ; orbital and pancreatic diseases are the most. Ligneous conjunctivitis is a rare, chronic and recurrent conjunctivitis characterized by fibrinous pseudomembranes on the palpebral conjunctiva, but also on the gingiva, trachea-bronchial tract and female genital tract. It is an autosomal recessive inherited disorder with mutations in the plasminogen gene (6q26). Herein, we reported a girl with ligneous conjunctivitis who developed chronic pancreatitis due to IgG4-RD.

Method: A 7-year-old girl admitted with abdominal pain referring to the back. She was on follow-up for ligneous conjunctivitis for the last 2 years and had two pancreatitis attacks during last year. Her parents were second degree relatives and her plasminogen activity level was 17% (normal range 55-145%). She had been treated with systemic and topical fresh frozen plasma, topical heparin, short term topical steroids and surgical excision was done 3 times before. Subepithelial eosinophilic amorphous material accumulation with increased number of lymphocytes and neutrophils were observed in the excised specimen.

Results: In laboratory examination, leukocytosis with neutrophil predominance, mildly elevated amylase (191 U/L; increase to <2 times the upper limit of normal) and lipase (94 U/L, increase to > 3 times the upper limit of normal) were detected. She experienced cholangitis, pneumobilia, hepatitis, duodenitis and interstitial lung disease. Heterozygous mutation on PRSS-1 gene was detected for hereditary pancreatitis. Auto-antibodies were negative, but IgG4 was high (>150 mg/dL). She was diagnosed as a possible IgG4-RD according to diagnostic criteria and methylprednisolone and azathioprine were started.

Conclusion: To our knowledge, only one adult patient had ligneous conjunctivitis due to proven IgG4-RD was reported before. The exact pathogenesis of the IgG4-RD is unknown. Accumulation of IgG4 positive plasma cells in tissues are hallmarks of the disease and CD4 + cytotoxic T lymphocytes have been shown to play a major role in formation of fibrosis. In ligneous conjunctivitis, due to plasminogen deficiency, fibrin cannot break-down and abnormally accumulate in the body. Further studies are needed to determine whether there is a real association between the two diseases or just a coexistence in two case reports.

TP0624 | Hereditary angioedema

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Case report: Hereditary angioedema (HAE) is a rare disease characterized by recurrent, self-limited episodes of swelling involving the skin and the mucosa of the gastrointestinal tract and upper airway. The best characterized forms of HAE arise from deficiency or dysfunction of C1 inhibitor (C1INH); however, there are other forms of HAE in which C1INH is normal.

A previously healthy 16-year-old female was admitted at the emergency department of our hospital after she woke up with prominent edema of the superior lip (Picture 1). She had no history of trauma nor had any history of food allergy. At the physical examination, she had angioedema of the left side of the superior lip, without urticaria or signs of respiratory distress. She had started oral contraception (OC) 2 months before. Reviewing the family history, her mother at the age of 19 years old, started having self-limited episodes of subcutaneous and submucosal angioedema with 2-5 days of duration, that she associated to the beginning of OC and to the 2 pregnancies that she had had. Her grandmother died at the age of 24 with edema of the tongue. Our patient had normal C1INH, C1q and C4 values. With this presentation, a hereditary angioedema with normal C1 inhibitor was suspected. C1INH concentrate was administered with a poor response, with posteriorly perfusion of tranexamic acid and regression of the edema (Picture 2). She was discharged and further study was continued at our consultation. A genetic study was performed to identify a possible mutation in factor XII. A single heterozygous nucleotide substitution within exon 9(c.983C>A) of the FXII was identified.

The incidence and prevalence of HAE with normal C1INH is limited. Members of an affected family may be asymptomatic or symptomatic to varying degrees, with the beginning of the symptoms normally after puberty. Triggers for episodes of angioedema can include local trauma emotional stress and certain medications. Exogenous estrogens are the most consistently reported medication to worsen symptoms. There is still limited data on the effectiveness of different therapies for this subtype of HAE.

TP0625 | Role of immune inflammatory mediators in the pathogenesis of inflammatory and noninflammatory chronic abacterial prostatitis

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Background: Chronic abacterial prostatitis (CAP) is a common urologic condition with possible immune pathogenesis. This study assesses the relationship between tumor necrosis factor-α (TNF-α), interleukin-10 (IL-10) and prostaglandin E2 (PGE2) in patients with inflammatory (iCAP) and noninflammatory (nCAP) chronic abacterial prostatitis.

Method: The 72 patients with CAP and 36 healthy males age of 18-45 years were studied including iCAP (n = 36) and nCAP (n = 36) and a control group, respectively. The diagnosis was established by presence of specific complaints, microscopy and culture evaluation of ejaculate. Concentration of PGE2, TNF-α and IL-10 in sperm were determined by enzyme-linked immunosorbent assay. The prostatitis symptoms were scored according to the National Institutes of Health chronic prostatitis symptom index (NIH-CPSI).

Results: Compared with the control group, the CAP groups had significantly ($P < 0.05$) higher levels of TNF-α, PGE2 and significantly ($P < 0.05$) lower levels of IL-10 in sperm. Concentrations of TNF-α and PGE2 in sperm of the CAP groups were not correlated with NIH-CPSI scores ($P < 0.05$), while the level of IL-10 in sperm was negatively correlated ($P < 0.05$) with NIH-CPSI scores prostatitis symptoms. There were no differences between levels of PGE2, TNF-α, IL-10 and NIH-CPSI scores in iCAP and nCAP groups.

Conclusion: Increase in PGE2, TNF-α and decrease in IL-10 concentration characterize pathogenesis of CAP. Pharmacologic agents which impact these mediators should be considered for treatment of CAP patients.

TP0626 | LNA probes for detecting donor cell-free DNA in sera of solid organ transplant recipients

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Background: Although a significant success in treatment of organ transplant rejection has been achieved, cancer and infections are still significant cause of death among solid organ transplant recipients. The main reason of an increased risk of fatal complications is a long-term and intense immunosuppressive therapy leading to immune function deficiency. Certain individual physiological parameters can help to reconsider immunosuppressive regimen to provide reasonable therapy with reference to given patient. One of the promising approaches in this field based on monitoring of acute rejection markers.

Method: Cell-free donor DNA was suggested as the perspective noninvasive graft of the rejection biomarker correlating to biopsy results of recipients with acute rejection. However, existing PCR-based methods are not sensitive enough to detect and discriminate donor-specific alleles in the background of major DNA template. In order to rise sensitivity, we are suggesting a new application of previously reported approach based on locked nucleic acid (LNA) probes, which are annealing to DNA target, providing complete inhibition of probe-specific template amplification. Therefore, in the unbalanced mixture of DNA templates LNA probes designed to target short INDEL polymorphism inhibiting major DNA template, rising the sensitivity of reaction and making possible to detect single copies of target DNA of different genotype.

Results: In order to evaluate the analytical capacity of this method, we tested 10-fold serial dilutions of target DNA template in a presence of major probe-specific template. The method showed capability to detect target DNA being at $1/10^5$ ratio to major template (0.001%).

Conclusion: Our method is less complicated and costly compared to shotgun sequencing and droplet digital PCR and it is getting over the specificity and flexibility limitations of DNA-marker detection in sex-mismatched and HLA-mismatched transplantations.

TP0629 | Cancer-testicular antigens as a basis for the creation of personalized autologous vaccines for urothelial cancer

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Background: The problem of combating cancer remains a priority throughout the world. Cancer immunotherapy is one of the new, innovative directions in the treatment of urothelial cancer (UC). Creation of antitumor vaccines is a new, innovative scientific area that contributes to the increased efficiency of antitumor treatment.

Malignant transformed cells of some tumors express immunogenic cancer-testicular antigens (CTAs), which can be a target for immunotherapy. CTAs expression and its relationship with mutations in UC are poorly understood. The objective of the work is to conduct a comparative analysis of CTAs expression in various clinical forms of UC.

Method: 24 tumor samples with different degrees of invasion were studied: 18(75%) muscle-invasive (MIF) and 6 (25%) muscle—non-invasive (MNIF) forms of UC. The immunological method of examination on the FACS Canto II device (the study of the expression of the CTA by using the monoclonal antibodies) and statistical methods of data processing (SPSS program 23.0 for Windows - parametric and non-parametric criteria) were used.

Results: It was revealed that with the MIF UC expression of NY-ESO-1 was in 7 (38.9%); MAGE in 15 (83.3%); GAGE in 8 (44.4%) and BAGE in 9 (50%) cases. 2 samples had 4 CTAs (11.1%), 5-three of 4 CTAs (27.8%), 16 - expression of the one CTA was detected (88.9%). But with MNIF UC NY-ESO-1, MAGE and BAGE expressions were recorded in rare case (1 in each tumor-16.7%). GAGE-in 2 samples (33.3%), two CTAs - in 2 samples (33.3%), there were no CTAs in two. In 66.7% of cases one of the 4 studied CTAs was presented.

Conclusion: We have identified the most common mutations of UC cells as well as differences of mutations in different UC clinical forms that offers the greatest promise for timely trial of most effective treatment. CTAs expression on UC cells depends on its degree of malignancy, invasion and metastatic propensity. MIF UC cells express 1.5-2.5 times more CTAs compared to MNIF UC cells. The most stable expressed CTAs are MADE, BAGE and GAGE. The presence of CTAs expression on UC cells determines the prospect of its use to develop an active personalized biotherapy treatment for the purposes of antitumor immunity improvement in patients with high-grade UC.

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TP0630 | Hereditary alpha-tryptasemia due to a TPSAB1 gene duplication associated with multifocal sclerotic bone disease

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Case report Rationale: Alpha-tryptasemia affects 4%-6% of the population and is caused by allelic replications of the TPSAB1 gene. It is typically associated with allergic-type skin and bowel symptoms, as well as cardiovascular symptoms and “brain fog”. Generalized aches and pains are common, as are joint hypermobility. Bone abnormalities have not been previously described.

Methods: Bone abnormalities associated with alpha-tryptasemia are described in this clinical case report. TPSAB1 allelic analysis was performed by droplet digital PCR.

Case report: A 57-year-old presenting with numbness in her feet and intermittent bony pains at the age of 53 years old. MRI and nuclear medicine scans showed multiple sclerotic bony lesions in her pelvis, which had a partial symptomatic response to zoledronic acid (procollagen type 1 N peptide decreased from 43-53 to 10-20 mcg/L with treatment (normal range 15-95 μ/L). The patient also suffered from intermittent idiopathic urticaria responding to antihistamines, indigestion responding to ranitidine, and palpitations. Bone marrow trephine excluded malignancy, but an increase number of non-spindle-shaped CD2- mast cells were seen. KIT mutation screen was negative. Serum mast cell tryptase concentration was persistently raised at 17-20 ng/mL. Bone biochemistry, including parathormone and Vitamin D were normal. An allelic TPSAB1 duplication was identified by ddPCR.

Discussion: Mast cell disorders are known to predispose to osteoporosis, as well as vertebral compression fractures and in a few patients diffuse sclerotic changes. Bone disease in alpha-tryptasemia has not previously been described. This case highlights symptomatic bony sclerosis, which can be confused with metastatic disease associated with this condition.

Conclusion: The case highlights that bony abnormalities can be associated with hereditary alpha-tryptasemia. Further studies are required to substantiate this potential association.

TP0631 | Features of humoral immunity in adenoma and prostate cancer

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Background: Adenoma and prostate cancer are common diseases of the urogenital system in men over 40 years of age. With both diagnoses, the prostate is affected; however, the etiology of the disease is different. The purpose of this study was to study the characteristics of the humoral immunity in patients with adenoma and prostate cancer relative to the control group.

Method: 90 patients with adenoma, 47 patients with prostate cancer and 125 healthy individuals were examined. The determination of the content of immunoglobulins (IgA, IgM, IgG, IgE) in the serum was carried out by enzyme-linked immunosorbent assay using test systems of Vector-Best, Russia. Statistical data processing was performed using Statistica for Windows 8.0 application packages with determination of the median (Me) and interquartile range (C_{25}-C_{75}). The statistical significance of the differences was determined using the Mann–Whitney rank test $P < 0.05$.

Results: The total number of B-lymphocytes in patients with adenoma and prostate cancer did not differ from the control group. In

patients with prostate adenoma, there was a decrease in IgM relative to the control group. IgA values increased in patients with adenoma and prostate cancer in relatively healthy individuals, but the data were not statistically significant. With metastasis of prostate cancer (stage III-IV), a significant decrease in the number of B-lymphocytes and all studied immunoglobulins in patients with prostate adenoma and the control group is noted in the immune status.

Conclusion: B-lymphocyte counts and all immunoglobulins studied depend on the stage of prostate cancer, in case of progression of the malignant process and metastasis, a sharp decrease in all indicators is observed, which can be used as an immunological monitoring in an oncological clinic.

SUNDAY, 2 JUNE 2019
TPS 02
ASTHMA: BIOMARKERS

TP0632 | Metabolomics reveal serum HETEs levels are correlation with allergic asthma in children: Three years drug and allergen immunotherapy as evidences

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Background: The aim of this study was to investigate the serum lipid metabolomic differences between patients with allergic asthma and healthy controls, and analysis of changes in serum arachidonic acid metabolism in allergic asthma patients with conventional drug therapy and specific immunotherapy respectively.

Method: 49 patients with allergic asthma were enrolled in the asthma group, and another 15 healthy individuals were recruited as the healthy group. Serum was collected, sample pretreated and derivatized, and used for non-targeted lipid metabolomics detection and profiled by ultra-high performance liquid chromatography-quadruple-time of flight/MS (UHPLC-Q-TOF/MS). Then, based on eicosanoid-targeted metabolomics, the changes of serum target metabolites before and after conventional drug therapy were retrospectively analyzed and explored the dynamic changes of the serum target metabolites during the allergen-specific immunotherapy for three years.

Results: UHPLC-Q-TOF-MS detected 278 lipid metabolites using the +ESI model and found a suitable OPLS-DA model for distinguishing the asthma group from the healthy group (R2 = 0.556, Q2 = 0.953). Differential metabolite analysis showed that levels of arachidonic acid (especially HETEs) in the asthma group were significantly higher than those in the healthy group ($P < 0.05$). From the ROC curve, it can be concluded that the differential metabolite with the largest area under the curve (AUC) is 12(S)-HETE (AUC = 0.983, 95% CI = 0.941-1.000). Therefore, most of the target metabolites (including 5-, 12- and 15-HPETE, 5-, 8- and 11-HETE) were significantly reduced after one year and three years of conventional drug therapy, and these important metabolite levels increased first and then decreased, 0Y was higher than 3Y, and 1Y levels were highest during subcutaneous injection immunotherapy (SCIT). Metabolic pathway enrichment analysis showed that differential metabolites are concentrated in arachidonic acid metabolic pathways, and this pathway is mostly associated with inflammatory reactions and oxidative stress. After conventional drug treatment, the target metabolite levels were significantly decreased ($P < 0.05$), and the LOX-mediated arachidonic acid metabolism pathway was significantly downregulated.

Conclusion: This suggested that HETEs were the potential biomarkers of asthma and Gpx4 might play important role in the regulation of the content of HETEs in asthma human serum, and may be used as biological indicators of therapeutic monitoring during SCIT treatment. Corresponding metabolic enzymes (COX and LOX), might be not only involved in asthma pathophysiology but also represent the therapeutic target for SCIT.

TP0633 | Childhood fractional exhaled nitric oxide as a predictor of asthma symptoms in adolescence

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Background: Asthma is a common disease in pediatric populations. It affects approximately 350 million people worldwide. Fraction of exhaled nitric oxide (FeNO) is recognized as a clinical marker of airway inflammation. However, it remains unclear whether childhood FeNO levels can be served as a predictor of subsequent asthma symptoms in adolescence. This study aims to investigate the relationship between childhood FeNO levels and subsequent asthma symptoms in adolescence.

Method: The study children were enrolled from the Prediction of Allergies in Taiwanese CHildren (PATCH) study, a prospective population-based cohort study launched in 2007. We measured FeNO level of each participant using a single-breath online method at enrollment, and employed a modified International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire to collect demographic data, general health information, and clinical data (e.g., clinical symptoms and diagnosis of allergic diseases) at enrollment and the 6-year follow-up, respectively. Multiple logistic regression models with covariates adjustment were carried out to evaluate the association of between childhood FeNO levels and longitudinal change of asthma symptoms in adolescence.

Results: A total of 1210 study children were included. Among those, there were 54 (4.5%) children without physician-diagnosed asthma at enrollment, but with physician-diagnosed asthma at follow-up, defined as incidence of physician-diagnosed asthma; 113 (9.3%) children with physician-diagnosed asthma at both enrollment and follow-up, defined as persistence of physician-diagnosed asthma; and 165 (13.6%) children with physician-diagnosed asthma at enrollment, but without physician-diagnosed asthma at follow-up, defined as remission of physician-diagnosed asthma. There were positive associations between FeNO levels at enrollment and

longitudinal change of asthma symptoms at follow-up (adjusted odds ratio (AOR) = 2.33, 95% confidence interval (CI):1.82-2.99 for wheeze ever; AOR = 2.39, 95%CI:1.60-3.56 for current wheeze; and AOR = 2.16, 95%CI:1.65-2.84 for physician-diagnosed asthma). Positive associations between FeNO levels at enrollment and persistent asthma symptoms at follow-up, including wheeze ever (AOR = 1.82; 95%CI:1.23-2.70), current wheeze (AOR = 2.30; 95%CI:1.06-4.98) and physician-diagnosed asthma (AOR = 1.73; 95%CI:1.01-2.96) were also observed.

Conclusion: Our results indicate positive associations between childhood FeNO levels and longitudinal change of asthma symptoms in adolescence.

TP0634 | Oxidative stress in asthma

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Background: Chronic airway inflammation is a major factor of asthma pathophysiology. The estimation of the airway inflammation in asthma is based on complicated and invasive methods: bronchial biopsies and bronchial alveolar lavage. Recently there has been an increasing interest in using exhaled breath condensate (EBC) as a non-invasive method of detecting different parameters of the airway, including oxidative stress biomarkers. Our aim was to estimate the oxidative stress in EBC in patients with moderate uncontrolled asthma (allergic and non-allergic) and to assess whether the intensity of that process may reflect the differentiation of asthma phenotypes.

Method: 44 patients (9 males, 35 females, age range 35-59 years) with chronic moderate asthma were included to the study. The diagnosis was based on clinical history, physical findings and lung function tests. 31 patients suffered from allergic asthma and 13 patients from non-allergic asthma. Both in blood serum, erythrocyte hemolysate and in exhaled breath condensate (EBC), the estimation of oxidative stress parameters was based on determination of: superoxide dismutase activity (SOD), protein sulfhydryl groups (SH), catalase activity (KAT), glutathione reductase activity (GR), glutathione S-transferase activity (GST), glutathione peroxidase activity (GPx), malondialdehyde (MDA), total oxidation status (TOS), total antioxidant capacity (TAC), lipofuscin, ceruloplasmin, lipid peroxides concentration (LPH).

Results: The oxidative stress markers were assessed both in peripheral blood and in EBC. On the contrary to peripheral blood, only 4 markers (TAC, TOS, KAT and GST) were detectable in EBC. There were no significant difference in level of those markers in EBC in patients with allergic and non-allergic asthma. The significantly higher oxidative stress parameters levels detected in blood of non-allergic asthma patients were observed with regards to CER ($P = 0.008$), LPS ($P = 0.04$) and MDA ($P = 0.014$). SH level in blood was higher in allergic patients ($P = 0.014$).

Conclusion: Asthma pathophysiology is directly associated with oxidative stress. The inflammatory process is increased among non-allergic asthma patients in comparison to allergic asthma patients. Exhaled breath condensate is only partially useful to assess airway inflammation.

TP0635 | NGAL (neutrophil gelatinase-associated lipocalin) and IL-5 (interleukin-5) potential biomarkers for asthma-COPD overlap differentiation from asthma and COPD

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Background: Asthma-COPD overlap (ACO) is a disorder that combines clinical signs of asthma (A) and COPD, fixed airways obstruction and/or significant bronchodilator reversibility, rapid progression, poor quality of life, higher mortality, frequent and severe exacerbations compared to COPD and A.

Method: 81 patients (Pts) with broncho-obstructive diseases out off exacerbation were studied: A (n = 26), COPD (n = 25) and ACO (n = 30). We determined the plasma levels of NGAL, IL-5 (ELISA) and blood eosinophils (Eo). Respiratory function and bronchodilator responsiveness were measured by standard spirometry.

Results: NGAL levels were significantly increased in ACO (158.6 ng/mL) compared to COPD (125.1 ng/mL) and A (53.5 ng/mL) ($P < 0.05$). Elevated NGAL levels were associated with a positive bronchodilator response (post FEV1/FVC < 70% and FEV1 ≥ 15% and ≥ 400 mL or ≥ 12% and ≥ 200 mL) ($P < 0.05$) and Eo count (Eo ≥ 300/μl) ($P < 0.05$) in ACO. IL-5 levels were significantly increased in A (4.48 pg/mL) compared to COPD (2.62 pg/mL) and ACO (2.53 pg/mL) ($P < 0.05$). Interesting, IL-5 levels did not match to high levels of NGAL ($P > 0.05$) and Eo (Eo ≥ 300/μl) ($P > 0.05$) in ACO.

Conclusion: Plasma levels of NGAL are significantly increased in ACO and are associated with blood eosinophilia, while plasma levels of IL-5 are significantly increased in A. These results suggest that plasma levels of NGAL may be useful biomarkers for differentiation Pts with ACO from COPD and A, and plasma levels of IL-5 may be a useful biomarker for A Pts.

TP0636 | Biomarkers of severe eosinophilic asthma: The role of induced sputum eosinophils, FeNO and blood eosinophils

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Background: In the past years, novel biological treatment options for severe asthma have emerged. In order to be able to offer these therapies to the suitable patients, it is mandatory to characterize these patients by detailed phenotyping. Several new agents are used in the treatment of severe eosinophilic asthma, which makes it important to demonstrate eosinophilic airway inflammation. The purpose of this study was to evaluate if the standard blood sample eosinophilic granulocyte count corresponds to the measurement of the fraction of exhaled Nitric Oxide (FeNO) and induced sputum eosinophils.

Method: We retrospectively evaluated blood eosinophils, FeNO and sputum eosinophils in 58 consecutive patients, where induced sputum was obtained. Results for these biomarkers were evaluated by dividing results in those in the normal range and increased values. Relative risk ratios (RR) and odds ratio (OR) were then calculated.

Results: Correlations between FeNO and blood eosinophils and FeNO and sputum eosinophils were not statistically significant. Correlation between blood and sputum eosinophils was observed: RR of 2.45, P = 0.01 and OR 6.07, P = 0.006. Inversely there was still a 16% risk of having a positive sputum sample when the blood eosinophilic count was normal; this was the case in 7 of 45 patients. These individuals represent a group who would not be offered biological treatment for severe eosinophilic asthma, potentially beneficial to them.

Conclusion: Eosinophilic sputum count is an important biomarker in severe eosinophilic asthma and may identify patients suitable for biological treatment, who are not detected by measurement of blood eosinophils or FeNO.

TP0637 | Sputum cytokine profiling according to different asthma sub-types

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Background: Asthma phenotyping is an important approach to separate more homogeneous asthma sub-types. This approach is not only useful in differentiation between various asthma mechanisms (endotypes) but is also a prerequisite for a personalized medicine and an improvement of treatment efficacy. The aim of the study was to characterise different types of asthma 1) atopic vs nonatopic 2) eosinophilic vs noneosinophilic based on sputum cytokine profile.

Method: Induced sputum (IS) was collected from corticosteroid naïve patients with mild-to-moderate asthma (n = 30). Total and differential cell counts in IS were assessed and the concentration of 35 cytokines were measured in sputum supernatant by Luminex platform or ELISA assay. Spirometry and bronchodilator reversibility was performed. Atopy was assessed with skin prick testing. Total IgE was measured in serum. Eosinophilic sub-type was defined as IS eosinophil percentage ≥ 3%. Atopic sub-type was defined as the presence of at least one positive skin prick test.

Results: We did not find any differences in cytokine level between eosinophilic vs noneosinophilic sub-type. IL-1β was the only cytokine differentiated atopic vs nonatopic asthma patients (median 3.41 vs 11.24 pg/mL, P = 0.01, respectively). Among atopic group total serum IgE level correlated positively with CCL24 (r = 0.56, P = 0.02), IL-6 (r = 0.57, P = 0.02), and IL-33 (r = 0.62, P = 0.01) concentration.

Conclusion: In mild-to-moderate asthma cytokine profile poorly distinguish between eosinophilic vs non-eosinophilic asthma and atopic vs non-atopic asthma.

TP0638 | Periostin and IL-10 in asthma and COPD

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Background: Periostin, a matricellular protein detectable in serum of patients with asthma has a strong association with disease severity. IL-10 is a cytokine that inhibits the production of pro-inflammatory cytokines in chronic inflammatory reactions. The aim of the study was the evaluation of relationships between serum periostin, IL-10 and clinical manifestation and severity of airflow obstruction in patients with obstructive airways diseases.

Method: Fifty patients (pts) (32 pts with asthma and 18 with COPD) were included in the study. The clinical evaluation included the presence of symptoms, the number of exacerbation in the last year and disease severity. Spirometry was also performed and the following parameters (VC, FEV1 and PEF) were recorded. Plasmatic levels of periostin and IL-10 were determined in all patients.

Results: Patients with COPD were older than patients with asthma (64.94 ± 6.95 vs 54.77 ± 12.77 years, P = 0.003). COPD was most frequently observed in males (70% vs 30%), while asthma was diagnosed frequently in females (80% vs 20% (P = 0.02). Periostin was significantly higher in patients with asthma [median 319.57 (257.1-463.69)] ng/mL versus COPD [median 171.19 (74.85-218.92)] ng/mL (P < 0.001). IL-10 was also higher in patients with asthma than in COPD [median 7.81 (1.13-62.4)] pg/mL versus COPD [median 0.47 (0-10.65)] pg/mL (P = 0.048). In patients with asthma, periostin was negatively correlated with patients' age (P = 0.05). Periostin was

positively correlated with asthma severity level (P = 0.027) and the number of exacerbation within last year (P = 0.05), while IL-10 was negatively correlated with disease severity (P = 0.034). Periostin was not correlated with spirometric parameters, while IL-10 was positively correlated with FEV1 (P = 0.047). In COPD patients, IL-10 was significantly lower in severe forms of disease (P = 0.05). Periostin was not correlated with disease severity or spirometric parameters.

Conclusion: Periostin and IL-10 had increased plasmatic levels in patients with asthma. Periostin may play a role in evaluation of asthma severity and clinical stage of disease, but not in COPD patients.

TP0639 | Clusters in Lithuanian asthma cohort study based on immune markers

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Background: Asthma heterogeneity has been revealed with the recognition of multiple pathways, mediators, and systems involved in triggering the characteristic airway inflammation and variable airflow limitation. Asthma can be divided into various distinct phenotypes based on clinical characteristics, physiological findings, and triggers. Usually, this way of phenotyping is a hypothesis-driven univariate approach. The other approach to phenotyping is utilizing computer algorithms to evaluate the hypotheses-free relationship between many clinical and biological characteristics.

Method: Cluster analysis was performed in R v3.5.0 using asthma patient data. A total of 170 adults patients with asthma (diagnosed according to recommendations of GINA) were recruited to the study. All patients underwent the following procedures: completed the questionnaires about their smoking history, physical examination, spirometry, skin prick test, blood sample collection to evaluate peripheral blood cells, serum IgE, periostin, and IL-33, as well as an assessment of body mass index. To minimize bias, smoking status and years of smoking were not included in the analysis. Data normality was checked with histograms and QQ plots. Hierarchical clustering was performed using Ward's linkage with Ward's clustering criterion. The optimal number of clusters was validated using the Dunn criterion as well as by comparing different clustering algorithms using the clValid package.

Results: Cluster analysis of our population revealed three clusters, one of whom included highly atopic patients, predominantly men, with early-onset of the disease, with normal lung function parameters and receiving low doses of inhaled CS. Moreover, the latter cluster is associated with very high levels of IL-33 and periostin, indicating their special role in eosinophilic inflammation. The second cluster could be described as late-onset, eosinophilic asthma with mild symptoms and normal lung function parameters. Finally, the third cluster is defined as late-onset, female predominant, obese, neutrophilic, with airway obstruction, treated with high inhaled CS doses, low IL-33 and periostin levels.

Conclusion: Analysis of Lithuanian asthma cohort study showed that patients vary by atopy, the age of disease onset, clinical, physiological, and inflammatory characteristics and three predominant clusters were identified. These inflammatory phenotypes can be further analyzed in selecting targeted therapeutics and identifying preventative strategies.

Characteristic	Cluster 1 (n = 43)	Cluster 2 (n = 84)	Cluster 3 (n = 43)	Adjusted R^2	P value
Age, years	32.59 ± 1.83	49.37 ± 1.52	55.58 ± 2.04	0.281	0.000
Sex, n (male/female)	32/11	16/68	10/33	NA	0.000
Age at asthma onset, years	28.02 ± 2.05	41.33 ± 1.84	43.29 ± 2.58	0.119	0.000
Asthma duration, years	4.21 ± 1.02	7.51 ± 1.26	13.02 ± 2.01	0.067	0.001
BMI, kg/m^2	25.47 ± 0.67	26.18 ± 0.52	30.01 ± 0.96	0.091	0.000
Treatment step$^{\#}$, 1-2/3/4-5	25/14/4	48/26/10	7/18/18	NA	0.000
Total IgE, IU/mL	720.31 ± 162.4	320.2 ± 61.5	482.86 ± 175.37	0.063	0.002
FEV_1, % of predicted	98.47 ± 2.55	97.11 ± 1.95	62.4 ± 2.63	0.434	0.000
FVC, % of predicted	105.58 ± 1.92	107.46 ± 1.7	81.67 ± 2.64	0.333	0.000
FEV_1/VC	77.05 ± 1.51	75.18 ± 1.14	58.3 ± 1.74	0.342	0.000
Serum eosinophils, ×10^9/L	0.48 ± 0.05	0.31 ± 0.03	0.29 ± 0.04	0.074	0.001
Serum basophils, ×10^9/L	0.05 ± 0.01	0.04 ± 0	0.03 ± 0	0.031	0.026
Serum neutrophils, ×10^9/L	3.55 ± 0.19	3.77 ± 0.14	4.94 ± 0.28	0.111	0.000
Serum lymphocytes, ×10^9/L	2.04 ± 0.07	2.13 ± 0.06	2.34 ± 0.13	0.019	0.075
Serum monocytes, ×10^9/L	0.55 ± 0.02	0.55 ± 0.02	0.63 ± 0.03	0.033	0.022
IL-33, pg/mL	1677.91 ± 276.39	371.29 ± 45.81	204.46 ± 41	0.134	0.000
Periostin, ng/mL	117.17 ± 13.09	60.41 ± 5.78	59.4 ± 6.23	0.068	0.001
Vitamin D, ng/mL	14.13 ± 0.96	14.67 ± 0.55	13.9 ± 0.66	−0.010	0.849

TP0640 | Biomarkers of eosinophilic airways inflammation in patients with severe asthma: A real-life study

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Background: Severe asthma is a heterogeneous disease consisting of different endotypes and inflammatory characteristics. Use of biologicals directed against T2 cytokines needs the validation of "Th2 endotype" in clinical practice using biomarkers, such as eosinophil count in sputum or blood, fraction of exhaled nitric oxide (FeNO), and immunoglobulin E (IgE). The aim of this study was to assess the biomarkers of eosinophilic airways inflammation in patients with severe asthma.

Method: We examined 71 outpatients (31% male, aged 18-82 years, mean age 55 years) with severe asthma according to ERS/ATS (2014) definition treated with high dose of ICS/LABA± tiotropium, antileukotrienes. Patients did not receive any biologicals for ≥ 6 months. Some patients (14%) had orally steroid-dependent asthma. Blood eosinophils (Eos) were measured by automatic haemoanalyser and serum total IgE levels were assessed by immunofluorescence assay. FeNO was measured by a chemiluminescence analyzer (Model LR4000; Logan Research, Rochester, UK). Eos ≥ 150 cell/μl, IgE ≥ 100 IU/mL and FeNO ≥ 25 ppb were considered as elevated markers.

Results: In patients with severe asthma level of blood Eos was 399 ± 53 cell/μl (8-3116 cell/μl) and 72% patients had Eos ≥ 150 cell/μl. FeNO was 33 ± 4.4 ppb (3-186 ppb) and 38% of patients had FeNO ≥ 25 ppb. Concentration of IgE was 370 ± 71 IU/mL (1-3596 IU/mL) and in 62% of patients level of IgE was ≥ 100 IU/mL. All three biomarkers were not elevated in 10% of patients with severe asthma. Ninety percent of patients had at least one or more elevated marker (Eos or IgE or FeNO). Increased blood Eos were the single marker in 17% patients with severe asthma, IgE—in 11% ($P > 0.05$) and FeNO — in 3% o ($P < 0.01$ compared with blood Eos). Two elevated markers (Eos ≥ 150 cell/μl and IgE ≥ 100 IU/mL) were diagnosed in 24%, Eos ≥ 150 cell/μl and FeNO ≥ 25 ppb - in 8% ($P < 0.01$), FeNO ≥ 25 ppb and IgE ≥ 100 IU/mL - in 4% patients ($P < 0.001$). All three elevated biomarkers were revealed in 23% of patients with severe asthma.

Conclusion: The majority of patients with severe asthma have at least one or more elevated biomarkers (blood Eos or IgE or FeNO) of eosinophilic airway inflammation. Eosinophil blood count is the most frequently elevated biomarker. There is an overlap between indications for prescription of different biologicals in patients with severe asthma.

TP0641 | Clinical characteristics of asthma according to blood eosinophil count

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Background: Asthma is a heterogeneous and chronic inflammatory disorder. Eosinophil is a major inflammatory cell involved in the pathophysiology of asthma. Sputum eosinophil is associated with disease severity, treatment outcome, and prognosis in asthma patients. However, it is less known of the relation between blood eosinophil and asthma. We investigated the clinical features of bronchial asthma according to blood eosinophil count.

Method: This retrospective study included a total of 121 asthma patients who visited the allergy clinic at Dong-A University Hospital from January 2014 to November 2018. We compared the clinical features of bronchial asthma, lung function and treatment response for 1 year according to initial blood eosinophil count: <300 cells/μL (group I, n = 54); 300-700 cells/uL (group II, n = 36); ≥700 cells/uL (group III, n = 31).

Results: Sputum eosinophil and fractional exhaled nitric oxide (FeNO) in group I was significantly lower than those in group II and III (5.83 ± 0.95 vs 22.73 ± 4.08 vs 17.56 ± 23.0%, $P < 0.001$ for sputum eosinophil; 25.02 ± 21.22 vs 61.5 ± 49.49 vs 60.17 ± 46.22 ppb, $P < 0.001$ for FeNO). Baseline pre-bronchodilator FEV_1 was no significant differences among three groups (68.88 ± 21.38 vs 69.39 ± 18.68 vs 66.71 ± 26.68%, $P = 0.877$). However, pre-bronchodilator FEV_1 after 1 year was much increased in group II and III compared to group I (70.74 ± 20.32 vs 79.84 ± 18.09 vs 83.81 ± 21.25%, $P = 0.03$). Airway hyperresponsiveness at baseline was more common in group II and III (30.8 vs 62.1 vs 61.9%, $P = 0.035$). The proportion of patients with tapering or stop of inhaled corticosteroids (ICS) after 1 year was no significant differences among our three groups (53.8 vs 55.9 vs 46.7%, $P = 0.74$).

Conclusion: Asthmatic patients with elevated blood eosinophil count showed improvement in lung function for 1 year treatment. There was no significant difference in change of ICS dosage according to blood eosinophil count in asthmatics.

TP0642 | Does fractional exhaled nitric oxide predict non-specific bronchial hyperresponsiveness in childhood asthma?

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Background: The fractional concentrations of exhaled nitric oxide (FeNO) have been elevated only in subjects with atopic asthma which is common in childhood. Non-specific bronchial hyperresponsiveness (BHR) induced by methacholine is used to diagnose asthma,

but some children occasionally cannot co-operate spirometry for methacholine challenge test. We sought to determine if methacholine challenge test could be replaced by FeNO measurement.

Method: Two hundred and fifty-five children patients reporting symptoms consistent with asthma were included in the study. All subjects underwent a methacholine challenge test following the five-breath dosimeter protocol. FeNO was measured with a portable device (Nobreath: Bedfont, Kent, UK) just before the methacholine challenge. BHR was defined as positive when methacholine PC_{20} FEV_1 ($MChPC_{20}$) ≤ 16 mg/mL.

Results: Children with BHR had higher FeNO than children without BHR (39.5 vs 30.8, P = 0.016). Although there was correlation between $MChPC_{20}$ and FeNO (r = −0.1328, P = 0.0340), it was very weak. ROC curve analysis was performed if the diagnostic value of FeNO was equal to methacholine PC_{20} FEV_1. Area under the ROC curve (AUC) was 0.595 (P = 0.0075). When FeNO > 37, sensitivity and specificity was 44.93 and 72.65, respectively.

Conclusion: Since FeNO level has a different meaning from methacholine-induced bronchoconstriction, methacholine challenge test cannot be replaced by FeNO measurement. In our study, the two tests are mutually complementary in pediatric asthma.

TABLE 1. Characteristics of the subjects

Characteristics	Uncontrolled Asthma (n = 42)	Controlled Asthma (n = 38)
Age (year)	38.6 ± 12.2	40.8 ± 12.2
Group Age, n (%)		
≤ 20 years old	3 (7.2%)	0 (0%)
21-30 years old	10 (23.8%)	9 (23.7%)
31-40 years old	9 (21.4%)	8 (21.1%)
41-50 years old	11 (26.2%)	12 (31.5%)
51-60 years old	9 (21.4%)	9 (23.7%)
Sex, n (%)		
Male	8 (19%)	11 (28.9%)
Female	34 (81%)	27 (71.1%)
Family History of Asthma	30 (71.4%)	27 (71.1%)
History of Allergic Rhinitis	32 (76.2%)	27 (71.1%)
History of Atopic Dermatitis	16 (38.1%)	18 (47.4%)
Education levels		
Elementary School	-	-
Junior High School	1 (2.4%)	3 (7.9%)
Senior High School	22 (52.4%)	18 (47.4%)
Bachelor's Degree	18 (42.8%)	15 (39.5%)
Master's Degree	1 (2.4%)	0 (0%)
PhD Degree	0 (0%)	2 (5.2%)
Body Mass Index (kg/m^2)	26.1 ± 4.9	24.8 ± 4.1
Body Mass Index (kg/m^2), n (%)		
< 18.5	1 (2.4%)	1 (2.6%)
18.5-22.9	10 (23.8%)	13 (34.2%)
23.0-24.9	7 (16.7%)	8 (21.1%)
25.0-29.9	17 (40.4%)	10 (26.3%)
≥ 30	7 (16.7%)	6 (15.8%)
Asthma Control Test Score	14.3 ± 3.8	23.6 ± 1.8

TABLE 2. Serum periostin levels in controlled and uncontrolled asthma

	N	Median (Minimum-Maximum)	p
Uncontrolled Asthma	42	209.78 (85.86-15739.38)	0.424
Controlled Asthma	38	627.66 (83.47-15646.17)	

TP0644 | Periostin is not associated with clinical assessment of asthma control in allergic asthma

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Background: Allergic asthma as the most common asthma phenotype is characterized by the activation of T2-type inflammation producing periostin. Many factors can influence asthma control, including allergen exposure, which may vary greatly with climatic and seasonal changes. The Indonesia region as the Maritime Continent is characterized by a wet and a dry season which is different from other regions with four seasons. This study was aimed to see the difference of serum periostin level in controlled and uncontrolled allergic asthma.

Method: This is a cross sectional study using samples from allergic asthma patients who went to Allergy and Clinical Immunology Clinic, Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia, in January to April 2017. Asthma control was assessed clinically by using Asthma Control Test (score < 20 as uncontrolled asthma and 20-25 as controlled asthma). Serum periostin measured with Periostin ELISA Kit (Aviscera Bioscience, California, USA) was used as biological markers reflecting Th2 inflammation.

Results: From 80 allergic asthma patients, the average of age was 39.7 years old with a greater proportion of women (76%). Most of the subjects had history of allergic rhinitis (73.8%) and positive family history of asthma (71%). House dust mites were the most common cause of sensitization. Forty two subjects were categorized as uncontrolled asthma (Asthma Control Test Score < 20). Serum periostin level in uncontrolled allergic asthma was not different from those in controlled allergic asthma (209.78 ng/mL vs 627.66 ng/mL, P = 0.424).

Conclusion: There was no difference in the level of serum periostin in controlled and uncontrolled allergic asthma.

TP0646 | Assessment of cytogenetic alterations in cells of asthmatic patients

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Background: The increased levels of chromosomal instability have been reported in a number of allergic and inflammatory diseases. At the same time the cytogenetic homoeostasis in the cells of asthmatic patients with different phenotypes have scarcely been studied in detail. The purpose of this study was to estimate the cytogenetic alterations in the cells of allergic and non-allergic asthmatic patients.
Method: The frequencies of chromosomal aberrations (CA) and sister-chromatid exchanges (SCE) in peripheral blood lymphocytes were scored for 70 (36 allergic and 34 non-allergic) asthmatic patients. The micronuclei (MN) frequencies in buccal epithelial cells were investigated for 56 (29 allergic and 27 non-allergic) asthmatics. The control group consisted of 20 healthy subjects.
Results: The significant ($P < 0.05$) elevation of CA and SCE frequencies as well as MN levels was revealed in the patients examined as compared with healthy controls. In patients with asthma exacerbation, SCE rates in allergic asthmatics appeared to be significantly ($P < 0.005$) higher than those in non-allergic ones; however, CA and MN levels did not differ ($P > 0.05$) in patients with different phenotypes. At the same time among the patients with stable asthma both CA and MN levels were found to be significantly higher in non-allergic asthmatics than those in allergic ones ($P < 0.05$), but no statistically significant differences in SCE frequencies were recorded in patients with allergic and non-allergic phenotypes ($P > 0.05$). Irrespective of the disease phenotype both CA and SCE levels were significantly ($P < 0.05$) higher in patients with asthma exacerbation than in stable ones. However, MN frequencies did not differ ($P > 0.05$) in cells from patients with asthma exacerbation and in those from patients with stable asthma.
Conclusion: The data obtained suggest that Asthma is a condition with increased chromosome instability characterized by a high levels of CA, SCE and MN frequencies. The cytogenetic alterations in cells of asthmatic patients depend on the asthma phenotype.

TP0647 | Serum level of eosinophil-derived neurotoxin: A biomarker for asthma severity in adult asthmatics

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Background: Eosinophilic inflammation is a key component of severe asthma (SA). However, there has been no reliable serum biomarker representing the eosinophilic inflammation of SA. We hypothesized that serum eosinophil-derived neurotoxin (EDN) might predict the eosinophilic inflammation of SA in adult asthmatics.
Method: Severe asthmatics (n = 235), non-severe asthmatics (n = 898), and normal controls (n = 125) were enrolled in Ajou University Hospital, Korea. Serum EDN and periostin levels were measured by ELISA, and we validated newly developed ELISA kit for serum EDN measurement, named K-EDN®. We compared the levels between severe and nonsevere asthmatics and evaluated their associations with multiple laboratory and clinical parameters of asthma. The predictability of serum EDN levels as a biomarker for SA was assessed.
Results: Severe asthmatics were older and had a longer duration of asthma with significantly lower levels of FEV_1 and methacholine $PC_{20,}$ compared to nonsevere asthmatics. Total eosinophil count and sputum eosinophil count (%) were significantly higher in severe asthmatics. Serum levels of EDN and periostin were significantly higher in severe asthmatics than in nonsevere asthmatics as well as healthy controls (all $P < 0.05$). Significant correlations were found in the result of serum EDN between the 2 kits ($\rho = 0.545$, $P < 0.0001$); a higher correlation coefficient was found between serum EDN levels measured by the K-EDN® and TEC ($\rho = 0.358$, $P < 0\ 0.0001$) than that of serum EDN levels measured by commercialized MBL® kit ($\rho = 0.319$, $P < 0.0001$). Serum periostin levels showed significant but less correlation to TEC ($\rho = 0.222$, $P < 0.0001$). Multivariate regression analysis showed that serum EDN levels measured by the K-EDN® could predict the phenotype of SA ($P = 0.003$), while other 2 eosinophilic biomarkers (serum eosinophil cationic protein and periostin) did not.
Conclusion: Serum EDN level can be a useful biomarker for predicting eosinophilic inflammation of SA in adult asthmatics.

TP0648 | The potential diagnostic value of periostin in patients with allergic bronchopulmonary aspergillosis

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Background: Allergic bronchopulmonary aspergillosis (ABPA) shares similar Th2 immune responses as allergic asthma, which lacks effective diagnostic markers. Periostin, a downstream protein of Th2 cytokine IL-13, has been reported to be a potential diagnostic or therapeutic target in asthma. Since there is no study on periostin in ABPA, our study aims to determine whether periostin level could characterize ABPA in patients with asthma and whether it could be an indicator during ABPA episode.
Method: Serum levels of periostin were analyzed by ELISA in 21 patients with asthma with ABPA, 23 asthma patients, and 13 non-atopic healthy individuals. Serum total IgE and fungal specific IgE were measured by ImmunoCAP in patients. The longitudinal course

of periostin and total IgE levels were assessed during ABPA episode. Additionally, levels of cytokines (IFN-γ, IL-5, IL-8, IL-10 and IL-17A) were measured by Meso Scale Discovery (MSD).

Results: The serum levels of periostin in ABPA patients (109.1 ± 68.28 ng/mL) were significantly higher than those in both non-ABPA asthmatic patients (57.39 ± 24.39 ng/mL) and healthy individuals (49.27 ± 8.37 ng/mL) ($P < 0.05$). Among the analyzed cytokines, ABPA patients had significantly higher levels of IL-5 and IL-8 compared with asthma patients (IL-5: 2.01 ± 1.432 pg/mL vs 0.57 ± 0.54 pg/mL, $P < 0.01$; IL-8: 73.31 ± 59.00 pg/mL vs 24.15 ± 27.00 pg/mL, $P < 0.05$). Correlation analysis showed that serum periostin levels was positively associated with total IgE levels ($r = 0.319$, $P < 0.05$), serum IL-5 levels ($r = 0.484$, $P < 0.01$) and blood eosinophil counts ($r = 0.428$, $P < 0.05$). ROC analysis showed that when periostin was applied for diagnosis of ABPA in asthma, the area under the curve was 0.705. Longitudinally, serum periostin levels reduced but not with statistical significance after treatment in relieved ABPA patients.

Conclusion: These findings suggested that higher levels of periostin related to profound Th2 immune inflammation. In addition, serum level of periostin may be a potential biomarker in the diagnosis of ABPA in asthma patients.

TP0649 | Personalized FeNO monitoring as a predictor of asthma control

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Background: FeNO level monitoring may be useful instrument for asthma diagnosis/treatment control. However, precise position of this biomarker for optimal asthma control is not defined now. The purpose of the study was assessment of personalized FeNO monitoring for asthma control level prognosis.

Method: There were included 111 uncontrolled bronchial asthma children (from 12 to 17 y.o.) after 3-month Step 2 (GINA) basic treatment and initial FeNO level ≥ 36 ppb. All patients were step-up therapy according to GINA and observed for next 3 months with monthly assessments of FeNO level (NOBreath, UK) and asthma control level (ACQ-test). Total group (n = 111) were divided into two subgroups (due to initial FeNO level): subgroup 1 (36 ppb ≤ FeNO < 50 ppb, n = 50) and subgroup 2 (FeNO ≥ 50 ppb, n = 61). FeNO predictive level for different asthma control (uncontrolled/partly controlled/ controlled) was assessed by ROC-analyze in total group and subgroups.

Results: There were no statistical significant relationships between 1-month FeNO level and 3-months asthma control status in all groups (total and subgroups). But we revealed predictive property of 2-months FeNO level in all groups. In a total group (n = 111) 2-months FeNO ≤ 28 ppb (ROC AUC = 0.7, $P < 0.0001$) was a predictor of asthma control in a 3 month of treatment. Two months FeNO > 28 ppb (ROC AUC = 0.73, $P < 0.01$) was a predictor of partial asthma control in a 3 month of treatment in a subgroup 1 (n = 50). Finally, 2-months FeNO ≤ 25 ppb (ROC AUC = 0.7, $P = 0.0003$) and 2-months FeNO > 38 ppb (ROC AUC = 0.67, $P = 0.02$) prognoses asthma control and partial asthma control in a 3-month of therapy respectively.

Conclusion: Two-months FeNO measurement may be optimal instrument for earlier step-up/down asthma treatment reassessment, earlier asthma control level achievement and improvement of asthma treatment results. Treatment tactics depends on the initial FeNO level and personalized methods developments are needed.

TP0650 | Inflammatory markers that binds receptor of advanced glycation end products(RAGE) in patients with asthma and ultrasound right cardiac findings

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Background: Asthma is a heterogeneous disease affecting 300 million approximately worldwide, and a chronic inflammation of bronchial airways. Receptor of advanced glycation products (RAGE) is a multiligand receptor of the immunoglobulin superfamily which upregulate pro-inflammatory pathways involving the pro-inflammatory transcription factor of NF-κB and it gets involved in many inflammatory diseases. Moreover, ultrasound right cardiac findings are scarce in patients with asthma.

Method: The study includes two groups. The first include 13 patients with bronchial asthma who were free of treatment for at least 2 weeks and the second 12 individuals without (control group).The diagnosis of bronchial asthma based on the international guidelines by GINA and a positive bronchodilator test after 400 μ salbutamol inhalation support the diagnosis of asthma. We receive plasma from all individuals and stored at −70°C for subsequent analysis and cardiac ultrasound demonstrated by a cardiologist. We investigate the levels of markers associated with the inflammatory load in the plasma of patients with bronchial asthma and we perform a cardiac ultrasound. Among the indicators to be studied are the following: soluble RAGE(sRAGE), S100A12(enRAGE), S100B, S100A8/A9 which were measured by ELISA (R&D Systems, Minneapolis, MN, USA). We use SPSS for statistic analysis.

Results: The aforementioned groups were similar among age, sex, body mass index and other comorbidities. Patients had 31% mild asthma, 54% moderate and 15% severe. All asthmatic patients had

TABLE 1. Inflammatory markers among groups

Markers	Patients	Control	*P* value
sRAGE (pg/mL)	216	371	0.090
enRAGE (ng/mL)	6.1	12.6	0.023
S100B (pg/mL)	227	166	0.573
S100A8/A9 (ng/mL)	1908	1131	0.301

a positive bronchodilator test at a mean change of FEV1" 370 mL and 12.4% and high level of FeNO(mean = 90.8 ppb). As for heart ultrasound, asthmatics showed less right ventricular volume than the control group which was statistically significant(29.6 mL vs 41.2 mL). While the inflammatory markers seem to play an important role among the groups, but only the levels of enRAGE was statistically significant (Table 1). When we separate the asthmatic patients base on phenotype(allergic or non) we find lower sRAGE, S100B and S100A8/A9 and higher enRAGE in allergic vs non-allergic but this was not statistically significant.

Conclusion: Asthma is an inflammatory disease of bronchial airways who do not affect the heart except from the volume of right chamber and new inflammatory biomarkers such as enRAGE are useful for diagnosis and follow-up those patients. The limitation of our study is the smal number of patients, so further studies required to clarify above results.

TP0651 | HETEs and prostaglandins distinguish asthma-COPD overlap from COPD by metabolomics study

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Background: The prevalence of asthma was more than 20% among individuals who had originally been diagnosed with Chronic Obstructive Pulmonary Disease (COPD), and for such patients it is assumed that Asthma-COPD Overlap (ACO)is associated with rapid progress and severe exacerbations. Physiological testing techniques are challenging, leading to misdiagnosis. This study aimed to apply a novel metabolomic approach to identify the metabolites in sera in order to distinguish ACO from COPD.

Method: In the study, blood samples were collected from patients with COPD, ACO and healthy controls between June 2017 and September 2017. (2-Aminoethyl)trimethylammonium chloride hydrochloride (cholamine)derivatization coupled with the ultrahigh performance liquid chromatography-quadrupole time-of-flight mass spectrometry (UHPLC-Q-TOF/MS)was used to investigate serum metabolites of eicosanoids. Statistical analysis approaches were applied to hunt for potential biomarkers in order to discriminate ACO from other diseases, as well as diagnose ACO.

Results: A clear intergroup separation was existed between the patients with ACO and those with COPD while ACO tend to have the higher serum metabolic levels of eicosanoids. A robust Bidirectional Orthogonal Projections to Latent Structures Discriminant Analysis (OPLS-DA)model was found for discriminating between ACO and COPD (R2Y = 0.81, Q2 = 0.79). The differential metabolites possessed higher values of area under the receiver operating characteristic (ROC) curve (AUC), suggesting an excellent biological marker for the prediction and identification of ACO. Furthermore, there is a significant correlation between some metabolites and clinical indicators, such as hydroxyeicosatetraenoic acids (HETEs) and FEV1/FVC, (prostaglandin F2α) PGF2α and BMI.

Conclusion: The metabolomic profiling of serum eicosanoids is able to clearly discriminate different biochemical metabolic profiles between ACO and COPD. The results may provide a new perspective to identify potential biomarkers of ACO and may be helpful for personalized treatment.

SUNDAY, 2 JUNE 2019
TPS 03
ASTHMA: DIAGNOSIS

TP0652 | The impact of GLI on spirometry interpretation in paediatric asthma

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Background: Spirometry is a fundamental test for the diagnosis and evaluation of lung function changes, as well as monitoring of lung function decline. The European Coal and Steel Community (ECSC) equations published in 1983 are still used in some centers, including in children. Currently, such equations do not suit all populations. The Global Lung Function Initiative (GLI), created in 2012, worked towards establishing new reference equations that could be applied in all ages. This study intends to determine the differences in spirometry results between ECSC equations and GLI equations in children and adolescents in a pediatric allergy consultation.

Method: Analysis of 51 spirometry records of patients with asthma, between 5 and 18 years old, performed in 2018. Z-scores and %predicted for FEV1 and FEF25%-75% were calculated using respectively GLI and ECSC reference equations. Low FEV1 values were defined as <80% and low FEF25%-75% as <60%. The calculations were executed using software provided by the GLI working group (www.lungfunction.org). Statistical analysis and comparison were performed using SPSS v.23.

Results: The rate of abnormal values was higher using GLI equations (12 patients) vs ECSC equations (3 patients). Nine patients with abnormally low results according to GLI equations had normal results when using the ECSC equations. This difference was statistically significant ($P = 0.004$).

Conclusion: As suggested in the literature and most recent guidelines, the use of GLI equations may have a significant impact on spirometry interpretation in pediatric clinical care. Patients previously considered controlled showed abnormal spirometric results with GLI equations. These new equations have potential to effectively standardize spirometry interpretation, benefiting future management and treatment of asthma in all ages.

TP0653 | Diagnostic performance of the methacholine versus mannitol bronchial challenge tests for diagnosis of bronchial hyperresponsiveness: A systematic review and meta-analysis

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Background: Bronchial hyperresponsiveness (BHR) is a representative feature of asthma. Although methacholine and mannitol are commonly used for bronchial challenge, the optimal roles of two agents' challenge in the assessment of BHR remain still unclear. We compared the diagnostic performances of methacholine and mannitol bronchial challenge tests.

Method: A systematic literature search was performed using MEDLINE, EMBASE, and the Cochrane Central Register. The sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic odds ratio (OR) and a summary receiver-operating characteristic curve (SROC) of two agents for diagnosing BHR were pooled using meta-analysis. A meta-regression analysis was used to identify potential sources of heterogeneity within the selected studies. BHR was defined as positive at PC20 < 16 mg/mL in the methacholine challenge and at PD15 of <635 mg in the mannitol challenge test, respectively.

Results: We identified eight studies comprising 970 patients. The pooled sensitivity, specificity, PLR, NLR and diagnostic OR of methacholine challenge were 0.64 (95%CI, 0.59-0.69), 0.80 (95%CI, 0.77-0.84), 5.60 (95%CI, 2.66-11.79), 0.36 (95% CI, 0.25-0.51) and 22.74 (95%CI, 7.21-71.73) respectively. The pooled sensitivity, specificity, PLR, NLR and diagnostic odds ratio of mannitol challenge were 0.54 (95%CI, 0.49-0.59), 0.85 (95%CI, 0.82-0.88), 8.39 (95%CI, 2.29-30.77), 0.55 (95% CI, 0.40-0.76) and 17.03 (95%CI, 4.42-65.56) respectively. The area under the SROC for methacholine was higher than that for mannitol (0.86 vs 0.64, $P < 0.001$). Although substantial between-study heterogeneity was found, none of the covariates were found to be potential sources of bias using meta-regression analysis.

Conclusion: We demonstrated that methacholine had better diagnostic performance than mannitol for diagnosing BHR, which would provide a better solution in the clinical practice of the diagnosis for asthma. However, because between-study heterogeneity was highly represented among the studies, our results should be interpreted with caution.

TP0654 | Does allergen susceptibility and allergen types affect the level of bronchial hyperactivity?

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Background: Allergen susceptibility can induce airway inflammation by the production of IgE antibodies in response to environmental allergens and may cause bronchial hyperreactivity (BHR). Although the perennial allergen sensitivity has been shown to be an increased risk for BHR, pollen sensitivity is controversial in BHR, except that it poses a risk for asthma. It is not known exactly whether the BHR level is affected by the type and variety of allergens. Objective: We aimed to investigate the presence of atopy and the effects of perennial, pollen and both types of allergen susceptibility on BHR in the presence of atopy.

Method: Within the last year, the data of patients who were admitted to our immunology and allergy clinic due to complaints such as breathlessness, wheezing, cough and spirometric measurements with normal methacholine and BHR test were analyzed retrospectively. Age, gender, prick test results, and methacholine concentration (PD20 value) with a 20% decrease in FEV1 were recorded. According to allergen type; 4 groups; nonatopic, perennial allergen, pollen and pollen + perennial allergen; According to the BHR level, four groups were formed: non-BHR, PD20: 8-16 mg/mL (mild), 4-8 mg/mL (moderate), 0-4 mg/mL (severe).

Results: A total of 324 patients (138 male, 186 female) with a mean age of 39.7 ± 13.7 were included in the study. While there were 123 (38%) patients with BHR (PD20.316 mg/mL), the atopy rate of these patients was significantly higher than those without BHR (56.9% vs 38.3%, $P = 0.001$). As shown in Fig. 1, it was observed that the majority of non-BHR patients were nonatopic, and those with mild BHR were often only pollen sensitive, while those with severe BHR were both perennial and pollen sensitive. ($P = 0.043$). According to allergen type, however, no significant difference was found between the groups in terms of median PD20.

Conclusion: BHR is associated with atopy and presence of atopy is a perennial allergen rather than a determining pollen allergen of BHR; The frequency and severity of BHR are increasing. This type of analysis will be indicative in the identification of asthmatic subphenotypes, progression of disease and phenotype-based therapy with more number of patients.

TP0655 | Cut-off value for Exercise induced bronchoconstriction

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Background: Recent asthma guideline recommends 10% fall in FEV_1 instead 15% as the criterion for exercise-induced bronchoconstriction (EIB). However, there is still controversy about the cut-off value for EIB.

Method: Medical records of 204 patents (7-63 year) who complained dyspnea after exercise and performed exercise challenge test were retrospectively reviewed. Patients were classified into three groups according to maximal % fall in FEV_1, as negative group (N) (<10%, n = 76), borderline EIB group (B) (10-15%, n = 45) and definite EIB group (E) (≥15%, n = 83). Symptoms after exercise challenge such as wheezing or cough, simultaneous significant(≥25%) decrease of FEF 25-75%, methacholine challenge results, exhaled NO and sputum eosinophil percentages were compared between groups.

Results: Wheezing after exercise challenge was very common in definite EIB group but rare in other groups (5.3% for N; 13.3% for B; 79.5% for E). Significant decrease of FEF 25-75% was also commonly observed in only definite EIB group (1.3% for N; 28.9% for B; 88.0% for E). Prevalence of bronchial hyperresponsiveness were different (25.8% for N; 52.6% for B; 84.1% for E), but average value of exhaled NO or sputum eosinophil percentages were not significantly different between groups.

Conclusion: Patients with borderline (10-15%) fall in FEV_1 after exercise challenge showed clinical features similar to negative EIB group rather than to definite EIB group. We suggest 15% fall of FEV_1 as an adequate cut off value for diagnosis of EIB.

TP0656 | Over or under-detection? A comparison of exercise and eucapnic voluntary hyperpnoea in the evaluation of exercise-induced bronchoconstriction

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Background: The most appropriate objective bronchoprovocation challenge in the evaluation of exercise-induced bronchoconstriction (EIB) remains debated. Standardising minute ventilation and environmental conditions during an exercise challenge test (EX) is problematic, whereas it has recently been proposed that eucapnic voluntary hyperpnoea (EVH) may be overly sensitive. The primary aim of this study was therefore to compare the airway response to EX in a dry environment (25% RH) and EVH. An evaluation of current and revised diagnostic thresholds was undertaken to determine the impact of any proposed modification to EIB screening outcome.

Method: In randomised order, sixty-three recreational athletes (male: $n = 47$) (training 9 ± 4 hrs/week) attended the laboratory on two separate occasions to complete either an EX challenge (6-min high-intensity cycling exercise at > 80% max heart rate) in an environmental chamber (16°C, 25% relative humidity), and a EVH challenge (6-min maximal ventilation of a dry compressed gas mixture: 21% O_2, 5% CO_2, N_2 balanced). Spirometry was performed at baseline and 3, 5, 7, 10 and 15 minutes post challenge test in accordance with international guidelines. A positive diagnosis was defined by ≥ 10% fall in FEV_1 at two consecutive time-points for both EX and EVH and ≥ 15% fall in FEV_1 at one time-point for EVH.

Results: The mean fall in lung function following EVH (-7.9 ± 6.9%) was greater in comparison to EX (-1.9 ± 7.1; $P < 0.01$). A moderate positive correlation was observed between tests ($\rho = 0.46$, $P < 0.01$); however, the mean bias was 6.1% and the data exhibited wide limits of agreement (+5.3 to −17.5%). Thirteen (21%) participants had a ≥ 10% fall in FEV_1 following EVH, of which five were positive to EX. Nine (14%) participants had a ≥ 15% FEV_1 fall following EVH, of which four were positive to EX.

Conclusion: Our findings indicate that EVH consistently induces a greater fall in FEV_1 in comparison to EX. Applying a 10% fall in FEV_1 cut-off for EVH results in greater diagnostic sensitivity, whereas a 15% fall in FEV_1 cut-off improves diagnostic specificity. Future population-based research evaluating the normative response to indirect bronchoprovocation in athletes remains a priority.

TP0657 | Induced sputum eosinophil and exhaled nitric oxide as tools for diagnosis of asthma

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Background: Induced sputum eosinophil (ISE) or fractional exhaled nitric oxide (FeNO) can be helpful for the accurate diagnosis of bronchial asthma.

Method: Data from 760 patients with asthmatic symptoms from 2015 to 2016 at a single tertiary center was analyzed. All the patients had records of methacholine bronchial provocation test (MBPT), ISE, and FeNO. Receiver operating characteristic curves (ROC) were analyzed to determine the best cut-off values of ISE and FeNO for the diagnosis of asthma.

Results: Two hundreds twenty three patients (29.3%) were diagnosed as asthma. The sensitivity of MBPT was 62.3% and specificity was 93.9%, with area under curve (AUC) of 0.820. ISE of asthmatics were significantly higher than non-asthmatics (median, 0.33% vs 7.2% $P < 0.01$). The best cut-off value of ISE was 2.7% with sensitivity of 65.6%, specificity of 84.5%, and AUC of 0.800. With combination of MBPT & ISE, the best cut-off value of ISE for asthma diagnosis was 5.7% with sensitivity of 80.8%, specificity of 90.0%, and AUC of 0.901. FeNO levels of asthmatics were higher than non-asthmatics (median, 60 ppb vs 22 ppb, $P < 0.01$). The best cut-off value of FeNO was 33 ppb with sensitivity of 70.5%, specificity of 76.2%, and AUC of 0.796. With combination of MBPT & FeNO, the best cut-off value of FeNO for asthma diagnosis was 51 ppb with sensitivity of 81.5%, specificity of 87.3%, and AUC of 0.902.

Conclusion: The sensitivity of MBPT was relatively low for the diagnosis of asthma. Concomitant measurement of ISE or FeNO resulted in the significant increase of sensitivity without compromising specificity. Both ISE and FeNO are useful in the diagnosis of asthma.

TP0658 | Is it clinical features or biomarkers in predicting asthma in wheezy children?

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Background: There is no laboratory test for predicting the development of asthma in wheezy children. The aim of this study is to evaluate the clinical features and the availability of serum periostin, osteopontin and YKL-40 biomarkers in predicting the development of asthma in children with recurrent wheezing in preschool period.

Method: In the study, the clinical features of the preschool age group with recurrent wheezing between the years 2011-2012 were evaluated, and levels of serum periostin, osteopontin and YKL-40 were measured. The same patients were re-evaluated in 2017 and their biomarker levels were repeated. The results of both age groups were compared with the control group.

Results: In this study, 197 patients with recurrent wheezing were evaluated. The mean±SD age of the patients was 3.33 ± 0.43 years. When the patients were re-evaluated after 5.89 ± 0.63 years, it was observed that asthma continued in 32% of them. No difference was found between patients with ongoing asthma and those in remission in terms of serum periostin, osteopontin and YKL-40 levels ($P > 0.05$). While there was no difference between the first and the final periostin values of the patients, the first osteopontin and YKL-40 values were found to be lower than the final values ($P < 0.001$). In addition, while the first osteopontin and YKL-40 levels of the patients were lower than those of the control group, there was no difference in terms of periostin. Final periostin, osteopontin and YKL-40 levels, however, were lower compared to the control group ($P < 0.05$). When multivariate logistic regression analysis was performed, it was observed that the risk of asthma continuing was higher in patients who had their first wheezing attack under 1 year of age, those with prenatal smoking exposure, preterm birth, cesarean delivery, wheezing without colds and multiple-trigger wheeze. [(Odd's ratio (95% CI, respectively): 5.125 (1.693-15.518) $P = 0.04$; 3.305 (1.555-7.024) $P = 0.002$; 4.884 (1.571-15.177) $P = 0.006$; 2.375 (1.078-5.229) $P = 0.032$; 3.628 (1.598-8.236) $P = 0.002$ and 4.732 (2.235-10.017) $P < 0.001$].

Conclusion: In our study, it was shown that clinical features were more valuable than biomarkers in predicting asthma in children with wheezing.

TP0659 | Airway remodeling and small airway disease

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Background: Airway remodeling and small airway disease (SAD) are key features of asthma. We aimed to compare non-eosinophilic (NEA) and eosinophilic asthma (EA) for remodeling and SAD.

Method: Patients were classified based on induced sputum criteria into EA (17 patients, 41% males, mean age 50.06 ± 11.85 years) and NEA (43 patients, 44% males, mean age 53.21 ± 14.20 years).

Bronchial remodeling was evaluated using high-resolution computed tomography (HRCT) with 5 regions of interest: upper edge of the aortic arch, tracheal carina, 1 cm below carina, inferior pulmonary veins and 2 cm above the diaphragm. Parameters assessed: bronchial wall thickening (BTW), wall thickness (WT), bronchial wall surface (WA), total bronchial area (AO), luminal area (AL).

Impulse oscillometry (IOS) was used to evaluate SAD. Parameters assessed: R5-R20, resonance frequency (Fres), reactance area (AX).

Results: Significant airway remodeling was revealed by HRCT in both EA and NEA (Table 1), with a trend for increased remodeling in NEA.

R5-R20, Ax and Fres were significantly increased in NEA compared to EA (Table 2).

Conclusion: Significant airway remodeling is present in both eosinophilic and non-eosinophilic asthma. The incidence of small airway disease is significantly increased in non-eosinophilic asthma.

TP0660 | Serology with specific IgE in children with asthma could lead to substantial cost savings for the NHS: A population-based simulation study

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Background: Asthma is the first cause of hospital admissions for children in the UK. As 65% of asthmatic children are sensitized to mites, dust-mite-impermeable encasings could reduce the burden of asthma. This study estimates the potential savings to the NHS, should allergy serology testing be performed in all asthmatic schoolchildren, and should interventions to reduce mites exposure be in place.

Method: In 2016, 8 669 085 pupils attended school in the UK; 788 099 of them were asthmatic and 512 264 sensitised to mites. Allergy testing (serology with specific IgE d1) in all asthmatic schoolchildren was simulated, to reduce exposure to allergy triggers in allergic individuals through house dust mite encasings. Model input parameters came from the literature; the modelled output, from the NHS perspective, were exacerbation-related hospital admission costs per year. Uncertainty was addressed with sensitivity analysis.

Results: In 2016, mites-related hospital admission costs were estimated in £ 611 896 729. The simulated intervention consisted in testing with d1 all asthmatic children (costing £ 88 858 163), and in the usage of house dust mite-impermeable encasings in all mites sensitised children (£ 0, no cost for the NHS). After the intervention, simulated total hospital admissions costs dropped to £ 432 011 928 in 2016. The total savings associated to the simulated intervention were £ 91 026 638 in the year 2016, and £ 105 098 890 in a 5-year time horizon (2016-2020).

Conclusion: A screening strategy based on serology with specific IgE in schoolchildren with asthma, in the UK, could hypothetically lead to substantial cost savings for the NHS due to reduced hospital admissions with asthma exacerbations.

TABLE 1. Bronchial remodeling parameters; first row mean ± standard deviation, second row variation interval

	WT (mm)	BWT(mm)	AO (cm^2)	AL (cm^2)	WA (cm^2)	WA (%)
Eosinophilic Asthma (n = 17)	0.94 ± 0.210.68 - 1.32	0.24 ± 0.030.18 - 0.29	12.33 ± 2.786.66 - 16.86	3.55 ± 0.811.79 - 4.76	8.98 ± 2.594.88 - 13.46	72.10 ± 6.8460.81 - 81.48
Non-eosinophilic Asthma (n = 43)	0.98 ± 0.230.64 ÷ 1.51	0.25 ± 0.040.17 ÷ 0.32	12.83 ± 3.787.63 ÷ 23.88	3.42 ± 1.331.44 ÷ 7.78	9.41 ± 3.105.41 ÷ 17.63	72.95 ± 7.4755.72 ÷ 86.84

TABLE 2. IOS evaluation; first row mean ± standard deviation, second row variation interval

	R5-R20 Pre-BD	R5-R20 Post-BD	Ax Pre BD	Ax Post BD	Fres Pre BD	Fres Post BD
Eosinophilic Asthma (n = 17)	0.56 ± 1.48-1.98 ÷ 4.17	1.12 ± 0.890.15 ÷ 2.89	13.47 ± 10.092.03 ÷ 28.11	10.83 ± 10.221.39 ÷ 36.40	18.05 ± 5.6510.73 ÷ 28.06	19.08 ± 7.4310.37 ÷ 34.34
Non-eosinophilic Asthma (n = 43)	1.94 ± 1.50**0.08 ÷ 6.32	1.62 ± 1.38-0.01 ÷ 5.53	24.30 ± 21.60*2.53 ÷ 104.34	18.83 ± 18.95*1.33 ÷ 70.68	24.99 ± 7.36**12.01 ÷ 39.79	22.26 ± 7.209.16 ÷ 36.45

*$P < 0.05$; **$P < 0.01$.

TP0661 | A novel asthma monitoring device studying symptomatic asthmatics during the first month of corticosteroid treatment

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Background: Monitoring the lung function of asthmatics relies heavily on peak flow and spirometry measurements which are forced manoeuvres and relatively difficult to perform. A novel Bluetooth and Cloud enabled asthma home monitoring device which uses a steady breathing technique to produce an Exhaled Breath Condensate (EBC_1) breath profile is in development. The breath profile is based on changes in the humidity of expired air as a result of airflow obstruction. A preliminary methacholine challenge study was successfully performed to validate the device performance and inform the implementation of this study. The primary objective of the study reported here was to compare the novel device with Spirometry in the evaluation of asthma symptom status in asthmatic patients during steroid treatment.

Method: One hundred steroid naïve asthmatics aged 18 to 80 were recruited. Participants were prescribed inhaled corticosteroids and monitored using spirometry, and the novel device. Monitoring took place at baseline and twice weekly for a total of eight visits. Analysis of 53 Participants which met the baseline criteria for further analysis is reported.

Results: Average demographic values of: 40.2 years old, 158.77 cm tall, 59.85 Kg, 48% females, all were Asian, FEV_1 values of 1.14 litres and PEF values of 2.51 litres were observed. Mean values for FEV_1, PEF and the EBC_1 prototype algorithm output from each visit were plotted and trendlines calculated on an individual Participant basis. Overall improvement or worsening of lung function according to each parameter were compared.

EBC_1 matched FEV_1 66% of the time. PEF matched FEV_1 68% of the time. Overall deterioration in lung function, as measured by FEV_1 was detected in 94% of cases using EBC_1. In the two cases of discrepancy the improvement in lung function over 4 weeks, as measured by EBC_1 were 1.19% and 0.45%. It is considered that refinement of the algorithm will remove these discrepancies.

Conclusion: The device (using EBC_1) was comparable to Peak Expiratory Flow in detecting changes to lung function tracked using FEV_1. These data suggest that EBC_1 could provide a viable alternative to peak flow meters for home monitoring. Further, it is considered that this could lead to improved compliance of home monitoring of lung function, as EBC_1 does not use the forced exhalation technique required for standard tests. The device and software are undergoing further development, with associated clinical investigations in the planning phase.

TP0662 | Clinical efficacy of information and communication technology based monitoring of asthma: A prospective, randomized controlled, multicenter study

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Background: Wide application of Information and Communication Technologies (ICT) to health care have allowed the development of tele-medicine based programs of care with chronic diseases. The aim of this study was to evaluation the impact of ICT based monitoring of asthma.

Method: We conducted a 6-month prospective randomized controlled trials for patients with asthma. Participants were centrally randomized to ICT group or control group. Primary outcome measures were changes of symptoms and quality of life, lung function. The ICT group provided ICT base monitoring system (daily recording and transmission of symptoms and FEV1, peak flow with immediate feedback promoting action according to an agreed plan). The control group was managing to visit the hospital every month.

Results: A total of 100 were enrolled. Ten were withdrawn from consent, resulting in 43 ICT and 47 control subjects. There was no difference in baseline characteristics. There was no significant difference in the change of symptoms score, quality of life, lung function between the two groups. The numbers of patients who had acute exacerbation was lower without significant in ICT group (4 vs 12, $P = 0.056$). There was no statistically significant difference in drug compliance. The cost of hospitalization and transportation was low in the ICT group, but the total cost was higher in the ICT group because the cost of monitoring system was high in the ICT group.

Conclusion: This study did not demonstrate significant differences in asthma related outcomes between two group. The ICT based monitoring system was no cost effective.

TP0663 | Bioluminescence analysis of saliva as non-invasive evaluation assay of physical exertion in human

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Background: The study involves the use of bacterial luciferase and NADH: FMN-oxidoreductase (BLuc-Red) in non-invasive assessment of physical exertion in athletes.

Method: Saliva samples collected before and after exertion from professional athletes (freestyle wrestlers, group 1, n = 25) and students (group 2, n = 25) served as sample for the study. The

bioluminescent test was used as the main research method, as a result of which the percentage of residual luminescence (T) of the bioluminescent system was determined. To explain the mechanisms of the bienzyme BLuc-Red system under the influence of saliva, its composition was studied during exercise: physical indicators (pH), chemical (Ca2 + , Na +, K +, Mg2 +) and biochemical indicators (total protein, lactate, catalase) and a correlation was made with the indicator T.

Results: A significant increase in T values was found for participants in the group 1 relative to the group 2 ($P < 0.05$) after exercise. At the same time, after exercise in both groups, the change in T depended on the activity of catalase, which decreased for participants in the group 1 and increased in the group 2. Influence of pH or ionic composition of saliva on the bienzyme system was not identified. Thus, the change in the bioluminescent luminescence of the enzymatic system, which occurs under the influence of catalase activity in saliva, can serve as an indicator of the physical exertion produced by the athlete's body.

Conclusion: The proposed bioluminescent analysis of saliva promises quick, non-invasive and easy-to-use monitoring of the physical condition of an athlete. This study was supported by Krasnoyarsk Regional Fund of Science according to the research project "Development of an express integral method for assessing the athlete's functional state with the aim of effectively managing the training process to achieve a high sports result".

TP0664 | Romanian experience behind awareness and screenings campaigns on the world asthma day in the last 4 years

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Background: For 8 years, on World Asthma Days, Romanian Society of Pneumology (SRP) organized an awareness campaigns consisting of press conference, radio campaign, dedicated website, free testing (spirometry) for general public in Bucharest. The aims of this study were (1) to identify subjects with airflow limitation, (2) to assess the relationships between the severity of symptoms and spirometry values.

Method: A retrospective, observational cohort study using spirometry and questionnaire tests was performed in the last 4 years. The questionnaire has 17 questions and addresses different issues like possible suggestive symptoms, risk factors, previous lung function tests, history of exacerbations, existence of any inhalatory therapy. Statistical analysis has been done using Microsoft Office Excel 2007.

Results: A total of 1173 persons screened by spirometry were notified as follows: 30.2%(355) in 2015, 27%(316) in 2016, 18.4%(216) in 2017 and 24.4%(286) in 2018. The demographic characteristics were: mean age = 56.7 ± 17.6 years, but most of them had over 61 years old in each year (due to the frequency of symptoms in this age group), males represented 54.5%(640), only 43.6%(512) with smoking history. From symptomatic ones 31.4%(369) had dyspnea, 40.8%(479) cough, 25.8%(303) chest tightness and 27.3%(321) wheezing. Although 46.1%(541) were symptomatic with normal spirometry, lung function impairment was detected in 20.3% (72/355) cases - 2015, 24% (76/316) - 2016; 22.2%(48/216) - 2017 and 28.7%(82/286) - 2018. Questionnaire analysis revealed that 19.8%(233) of patients had been diagnosed with asthma, just 10.2% (120) had actually treated their disease and 9.2% (108) of them had performed spirometry in the last 6 months.

Disease severity: 4.3%(50/1173) cases had presented to the emergency room in the last year due to the worsening of the pulmonary symptoms and 9.8%(116/1173) had limitation of daily activity secondary asthmatic disease.

Conclusion: Treating asthma is deficitary, pulmonologists was responsible for managing asthma in 10.3%(121) cases, while allergologists in 3.2%(38) cases. Asthma awareness campaigns based on case findings (questionnaires plus spirometry) are useful for detecting new cases, but also for already diagnosed cases, who were not followed up properly, regarding treatment or assessing asthma control.

TP0665 | Air pollution, lung function and inflammatory markers in adult asthma based on land use regression, inverse distance weighting and kriging Method

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Background: A 2016 World Health Organization (WHO) report shows that 92% of the world's population currently live in areas where air quality levels exceed WHO limits. In addition to traffic exposure and emissions from industrial areas, several studies have also pointed out that Chinese fast-food habits and religious beliefs in burning incense can also cause harm to air quality. As an industrial town of Taiwan, Kaohsiung City has the highest density regardless of population density or factories Under the influence of such economic industries, although it promotes the development of Kaohsiung City, it also affects the quality of life of Kaohsiung residents. Therefore, this study explored the effects of air pollution on lung function and inflammatory indicators in Kaohsiung asthma patients.

Method: This study mainly collected air pollutants data on O_3, PM_{10}, $PM_{2.5}$, NOx, NO and NO_2 from 12 air quality monitoring stations in Kaohsiung area from 2014 to 2016. The digital information of major roads, rivers, industrial areas, coal-fired power plants, temples, night markets, temperature and humidity, transportation and population density were collected to establish a land use regression model. We used inverse distance weighting (IDW), Kriging method and the land use regression model (Land-use Regression) to estimate the

air concentrations for 347 asthma patients from Kaohsiung Chang Gung Hospital. We applied multiple linear regression to investigate the effects of air pollutants on the health effects of asthma patients.
Results: In this study, we found that long-term exposure to PM_{10} and $PM_{2.5}$ have relatively consistent impairments in lung function, especially for FEV_1 and $MMEF_{75/25\%}$. In the analysis of health effects of nitrogen oxides, it was found that the increase concentrations of nitrogen oxides have significant effects on neutrophils (b = 1.767, 95% CI = 0.23-3.30 by LUR; b = 1.340, 95% CI = 0.02 = 2.65 by Kriging; and b = 1.767, 95% CI = 0.23-3.30 by IDW, respectively).
Conclusion: We observed an increase in air pollutant concentrations in Kaohsiung, which may significantly lead to an increase in neutrophils and a decrease in lung function in asthmatic patients. These findings indicated that exposure to long-term air pollutants can have an impact on health in asthmatic patients.

TP0666 | Long term follow-up of cough variant asthma

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Background: Normal lung function with presence of BHR is a diagnostic conditions in cough variant asthma. Sometimes patents with cough variant asthma visit with dyspnea and showed reduced lung function, then re-diagnosed as a typical asthma during follow up. We tried to find the difference of clinical characteristics between subjects with reduced lung function and with remained in normal lung function.
Method: The cough variant asthma was defined by ACCP guidelines including chronic cough more than 8 weeks, normal FEV1, positive methacholine inhalation test, and good response of inhaled steroid therapy. 1662 patients were diagnosed as CVA. Among 1662 CVA patients, 284 patients were revisited to hospital with symptom of chest tightness.
Results: Of the 284 subjects, fifty two (18.3%) patients showed reduced FEV1. Mean interval between diagnosis of cough variant asthma and reducing of FEV1 was 305.5 days. There was no significant difference of level of PC20 or other pulmonary functional values between FEV1-reduced group and -preserved group.
Conclusion: Most of the cough variant asthma still preserve their lung function to be in normal range, only small portion of patients was transformed to asthma with reduced FEV1.

TP0668 | Peak expiratory flow versus spirometry for diagnosis of asthma in adults

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Background: The diagnosis of asthma is clinical and is confirmed with a FEV1/FVC ratio < 80% and reversibility of FEV1 > 12% and 200 mL, after the use of salbutamol during spirometry. Peak expiratory flow (PEF) is cheap and easy-to-use tool that measures the forced or maximum expiratory flow (FEM), its reversibility > 20% suggests asthma.
Objective: To know the sensitivity, specificity and negative positive and negative predictive values PEF
Method: Methods: cross-sectional, observational, comparative study. The calculation of size was made with biostasts Calculator 2014 for simple sample, assuming a sensitivity > 80% for PEF. The sensitivity, specificity and negative positive and negative predictive values OF PEF were calculated.
Results: 150 patients were included, 66% corresponded to men and 34% to women, the median age was 38 years (28.50). According to the control levels of GINA, evaluated by ACT, 58.7% was controlled. The mean FEV1 in asthmatics was 73% (16) and for non-asthmatics 88% (13), the average FVC in asthmatics was 81% (13) and in non-asthmatics 88% (14). The FEV1/FVC ratio in asthmatics was 80% (14) and in non-asthmatics 87% (17) with $P = 0.00$. The median PEF measured by flowmetry in asthmatics was 370 mL (290, 430). PEF sensitivity was 47% and specificity 87%, with a positive predictive value of 54.8% and the negative predictive value of 84%. PEF showed greater specificity with FEV1 < 59%.
Conclusion: diagnosis of asthma remains clinical, both, a spirometry-PEF normal do not rule out the diagnosis.

TP0669 | Impact of ban of humidifier-disinfectants-sales on preschool asthma in Korea: A nation-wide interrupted time series

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Background: Environmental toxicants (ET) are risk factor for the asthma. Although evidence suggests important risk of exposure to ET in early life, the impact on the asthma is still unclear. In Korea, sales of humidifier-disinfectants were banned due to the causal inference between use of HDs and fatal acute lung injury since November 2011. This study aimed to investigate the cessation effect of HDS on the asthma-related outcomes in preschool children.
Method: Health Insurance Review and Assessment Service data were used to identify all health-care related information for asthma in Korea from 1 January 2007 to 31 December 2015 among whole Korean population under the 6 years of age. Interrupted time series with generalized estimating equation was used to investigate the cessation effect on the risk of asthma-related hospitalization,

emergency-department (ED) visit, and ranks-sum of asthma-medications (based on the stepwise approach in the GINA guideline) before and after the ban of sales.

Results: We studied 817 809 preschool asthmas. Ban of HDS-sales was associated with an immediate 7.4% (Adjusted odd ratio, 0.926; 95% CI 0.883-0.971) reduced risk of asthma-hospitalization, and 49.1% (aOR, 0.501; CI 0.480-0.524) reduced in ED visits rate after adjustment for sex, age, birth seasons, lower respiratory tract infections. The ranks-sum of asthma medications was immediately 22.9% reduced (aOR, 0.771; 95% CI 0.759-0.783). In addition, it was associated with sustained reduction in asthma-hospitalization (6.4% per year; aOR, 0.936; 95% CI, 0.912-0.960), 10.0% per year in ED visits (aOR, 0.900; 95% CI, 0.839-0.966), and 26.1% per year in ranks-sum of asthma-medications (aOR, 0.739; 95% CI, 0.716-0.762) during study-period.

Conclusion: Ban of HDs-sale was associated with immediate, and sustained reduction of all asthma-related outcomes, and ranks-sum of asthma-medications in Korean preschool children with asthma. The search for the modifiable or preventable risk, like as unexpected environmental factors, should be regarded as a public health priority.

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SUNDAY, 2 JUNE 2019
TPS 04
RHINITIS AND RHINOSINUSITIS MANAGEMENT

TP0670 | Allergic rhinitis (AR) therapy decisions during a routine consultation: A multicenter, cross-sectional study (AR therapy survey)

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Background: Therapy options for patients with AR depend on many factors, including symptoms, symptom severity and AR control. This study assessed physicians' therapy decisions and how these decisions are linked with previous therapies and current symptom severity.

Method: A total of 228 symptomatic patients (aged ≥ 12 years) from Hungary were assessed. Patient demographics, AR therapy within the last 7 days, AR therapy decision, symptom assessment by Visual Analogue Scale (VAS), and adverse drug reactions were recorded by physicians during a single visit. AR therapies were coded into Steps (1-4; Table), according to the MACVIA algorithm.

Results: Patients had a mean age of 42 years; 54% were female. Overall, 67% of patients had previous AR therapy and 35% of those had at least two AR therapies. Prior to the consultation, patients who had previous AR therapy and a VAS ≥ 50 mm were mainly on Step 1 (55%), regardless of previous AR therapy; 68%-75% of patients with a VAS ≥ 50 mm were prescribed AR therapy at Step 3 during the consultation (Table). Prior to the consultation, most patients who had previous AR therapy and a VAS < 50 mm were on Step 2 (49%); 43% were prescribed AR therapy at Step 2 during the consultation (Table). In total, 72% of patients who had previous AR therapy and a VAS ≥ 50 mm were stepped-up in AR therapy; however, nearly a third of patients (28%) were not stepped-up in AR therapy as recommended by the MACVIA algorithm. The most prescribed therapies at the consultation were intranasal corticosteroids (INCS; 49%) and a fixed combination of INCS and oral or intranasal antihistamines (42%).

Conclusion: This Hungarian study signified the real-life prescribing patterns for AR therapy among physicians. Patients with more severe symptoms and had previous AR therapy within the last 7 days were mostly stepped-up in AR therapy. However, a considerable number of patients still take multiple medicines before being moved to the next step of AR therapy. Further physician education to improve AR management and control is needed.

TP0671 | The efficacy of the fixed combination of mometasone furoate and azelastine hydrochloride as a nasal spray in adult patients with perennial rhinitis

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Background: Most patients with allergic rhinitis (AR) seeking for medical help suffer from moderate/severe persistent symptoms and

TABLE. AR therapy prescribed during consultation visit per step

Therapy decision step[1]	Patients with VAS ≥ 50 mm and previous AR treatment within last 7 days (n = 118)	Patients with VAS < 50 mm and previous AR treatment within last 7 days (n = 35)	Patients with VAS ≥ 50 mm and no previous AR treatment within last 7 days (n = 62)
No treatment	0	0	0
Step 1 (any therapy, excluding CS)	6 (5.1)	6 (17.1)	6 (9.7)
Step 2 (any intranasal CS, but not combined with oral/intranasal antihistamines)	22 (18.6)	15 (42.9)	14 (22.6)
Step 3 (fixed or free combination of intranasal CS and oral/intranasal antihistamines)	89 (75.4)	14(40.0)	42 (67.7)
Step 4 (any use of oral/nebulized steroids)	1 (0.8)	0	0

[1]According to Bousquet J et al. J Allergy Clin Immunol. 2016;138(2):367-374.
[2]AR, allergic rhinitis; CS, corticosteroids; VAS, Visual Analogue Scale.

use multiple treatment. An effective strategy for these patients may be using of a fixed combination of an intranasal corticosteroid (InCS) and a topical antihistamine drug. The objective of this study was to prove the efficacy of the fixed combination of mometasone furoate and azelastine as a nasal spray compared to the original drugs azelastine hydrochloride and mometasone furoate, used in combination with each other from separate nasal devices for control of nasal (TNSS) and non-nasal (TNNSS) symptoms of perennial allergic rhinitis (PAR) in adults.

Method: In total of 150 patients, 18-65 years of age, diagnosed with PAR having moderate/ severe symptoms were randomized in an open, parallel-group, multicentre clinical trial conducted in 10 centers in the Russian Federation in 2017.

Results: As a result of therapy with the study drug and comparative drugs, a significant reduction of all nasal and non-nasal symptoms was achieved, as well as an improvement in the quality of life of patients. The compared drugs did not differ. The fixed combination and comparators start to act very quickly. The fixed combination reduced the nasal and non-nasal symptoms within 5 minutes after the first application by 20% and 22%, by 47% both in 15 minutes and after 30 minutes by 65% and 59%, respectively. During the entire study period, adverse events (AEs) were detected in 15.33% (23/150) of the total number of participants in the study. Comparative analysis of AEs of all patients did not reveal a statistically significant difference between the groups of patients receiving the study drug or comparators.

Conclusion: Thus, the results of the study proved that the fixed combination of azelastine hydrochloride 140 μg + mometasone furoate 50 μg in the form of a nasal spray has no less efficacy and safety than the original preparations of azelastine hydrochloride - nasal spray and mometasone furoate - nasal spray, applied from the individual devices in adult patients with moderate /severe PAR. All patients noted the ease of use of the study drug.

TP0672 | Mometasone furoate plus isotonic nasal saline versus isotonic nasal saline alone in geriatric chronic rhinitis: An open-label, active comparator, randomized trial

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Background: Prevalence of diseases associated with aging is rising; among these are the rhinologic problems. Chronic rhinitis appears as one of the most common worrisome nasal disorders in this age group. At the same time, the allergic form diminishes because of the immunosenescence. This study aimed to evaluate the effect of a corticosteroid nasal spray (mometasone furoate) over nasal patency and the severity of rhinitis and its impacts on quality of life.

Method: This open label-trial randomized subjects ≥ 60 y with chronic rhinitis (allergic and nonallergic rhinitis) with mometasone spray 100 μ/d and isotonic saline nasal spray or saline alone for 2 weeks. The primary endpoint was the improvement in nasal patency evaluated by the peak nasal inspiratory flow (PNIF). Secondary outcomes included the severity of symptoms and the quality of life assessed by a visual analogic scale (VAS) and the sinonasal outcome test (SNOT-22), respectively.

Results: Forty patients underwent randomization, in equal number in each group of treatment, either with allergic (AR) and nonallergic rhinitis (NAR). At week 2, the mean PNIF score was 79.5 in the corticosteroid (CE) plus saline group and 82.0 in the saline group ($P = 0.37$). Also, SNOT-22 was not improved with the addition of mometasone furoate. An improving in the VAS score with the use of CE plus saline was observed in a subset of patients with elevated total IgE ($P = 0.07$) and in those with asthma ($P = 0.10$).

Conclusion: Treatment with mometasone furoate nasal spray plus isotonic saline is not superior to saline alone in elderly patients with rhinitis in respect of improving nasal patency, quality of life and reducing the intensity of symptoms. However, in those with asthma coexistence or total IgE elevated was observed significant differences in respect with improvement of VAS.

TP0673 | A multicenter study on the efficacy and safety of So-Cheong-Ryong-Tang for perennial allergic rhinitis

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Background: Allergic rhinitis (AR) is an inflammatory disease of the nasal membranes that results from an immunoglobulin E (IgE)-mediated allergic reaction. The prevalence of AR is 10-40% worldwide and 16.1% in South Korea. AR can be classified as seasonal (SAR, occurring during specific seasons) or perennial (PAR, occurring year round). The major symptoms of AR are nasal congestion, rhinorrhea, nasal itching, and sneezing. AR is not a life-threatening disease; however, it has a considerable impact on the patients' quality of life and causes social and economic burden. Furthermore, untreated AR is a risk factor for asthma, rhinosinusitis, nasal polyps, otitis media, and allergic conjunctivitis. So-Cheong-Ryong-Tang (SCRT) is a mixed herbal formula that is used to treat allergic rhinitis, bronchitis, allergic asthma, and common cold in traditional Korean medicine (TKM). To assess the efficacy and safety of the SCRT for the treatment of perennial allergic rhinitis (PAR).

Method: We conducted a double-blind, randomized, placebo-controlled, parallel-group, multicenter study of Korean adults with PAR. The trial consisted of a 4-week oral administration of SCRT or placebo, with two visits at 2-week intervals, and an 8-week follow-up period, with two visits at 4-week intervals. The primary outcome was a change in the total nasal symptoms score. The secondary outcomes included

TABLE 2. Components, standard materials, and TM action of SCRT

Botanical name	Herbal name	Amount*	Standard materials
Ephedra sinica Stapf	Ephedrae Herba	0.5	Ephedrine
Cinnamomum cassia Blume	Cinnamomi Ramulus	0.2	Cinnamaldehyde
Asiasarum sieboldi F. Maekawa	Asari Radix	0.5	Asarone
Zingiber officinale Roscoe	Zingiberis Rhizoma	0.5	6-Gingerol
Schisandra chinensis (Turcz.) Baillon	Schizandrae Fructus	2.67	Schizandrin
Paeonia lactiflora Pall.	Paeoniae Radix Alba	1	Paeoniflorin
Pinellia ternata Breitenbach	Pinelliae Rhizoma	2.67	Homogentistic acid
Glycyrrhiza uralensis Fischer	Glycyrrhizae Radix	1	Glycyrrhizic acid

*g, per day dose (9 g)

changes in the Rhinoconjunctivitis Quality of Life Questionnaire score, total serum immunoglobulin E (IgE), cytokines levels, nasal endoscopy index, and pattern identification (PI) by clinicians.

Results: SCRT improved nasal symptoms and quality of life in patients with PAR after 4 weeks medication, and these effects did not last 8 weeks after the end of medication. The level of serum IgE, eosinophil counts, and cytokines did not alter after medication. Nasal endoscopy index and PI by clinicians did not show significant difference. No serious AEs and safety assessment changes were observed in this trial.

Conclusion: SCRT is an effective and safe medication for patients with chronic, perennial, and moderate to severe AR. A clinical study with a > 4-week period of medication use, a standardized PI questionnaire, and more participants for immune material test is needed to investigate the long-term efficacy of SCRT in relieving the symptoms of nasal obstruction and identifying the underlying mechanisms of action and indications for TKM.

TP0674 | Algorithm for allergic rhinitis treatment based on the use of powder hydroxy-propyl-methyl-cellulose sealant

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Background: Powder hydroxyl-propyl-methyl-cellulose (pHPMC) has been traditionally used in subjects with allergic rhinitis as barrier enforcing measure to prevent the contact of the nasal mucosa with inhaled allergens. We have also demonstrated that pHPMC insufflated intranasally in subjects with rhinitis symptoms after other locally applied drugs prolongs and enhances their pharmacological effects. Based on this effect of pHPMC and on the leading individual symptoms of the patients, we have developed an algorithm for allergic rhinitis management. We present now a proof-of-concept study to substantiate this algorithm.

Method: We instructed 22 patients sensitized to grass pollen to treat their in-season symptoms by intra-nasal drugs following a set of simple recommendations: squirt oxymetazoline if nose is totally plugged; squirt azelastine if rhinorrhea/itching/sneezing are prevalent; squirt mometasone if all symptoms are flourishing. Patients could also make different mixes of these drugs. Patients were randomized to use after any application drug or mix of drugs a puff of either HPMC or powder lactose (placebo) to seal their combined effect. Subjective symptoms were assessed by visual-analogue scale (VAS). The pre- and in-season objective outcomes were peak nasal expiratory flow (PNIF), saccharine test (ScchT) and exhaled breath temperature (EBT, a surrogate marker of airway inflammation). The before-/in-season differences were computed and compared.

Results: The before-/in-season differences for PNIF and EBT favored the HPMC using group vs placebo users: PNIF -53.3 ± 0.06 (mean±s.e.m.) vs -26.5 ± 0.04[L/min], $P = 0.037$; EBT 0.24 ± 0.15 vs -0.46 ± 0.20[°C], $P = 0.010$. There was no statistical difference for ScchT ($P = 0.448$). The likely interpretation is that HPMC augments the local therapeutic response by suppressing symptoms, nasal congestion (PNIF) and airway inflammation (EBT), while still preserving normal cilia beat (ScchT).

Conclusion: An algorithm for management of symptoms in patients with seasonal allergic rhinitis using HPMC as a sealant of nasally applied drugs brings about significant clinical benefit.

TP0675 | Effect of yoga training on nasal blood flow and symptoms in allergic rhinitis patients

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Background: Allergic rhinitis is an inflammation of the nasal mucosa in response to allergens. There is evidence that yoga can improve

personal health and has positive effects on immune function. However, the effects of yoga training on nasal blood flow and symptoms in patients with allergic rhinitis are still unclear. The purpose of this study was to investigate effects of yoga training on nasal blood flow and symptoms in allergic rhinitis patients.

Method: Twenty-seven allergic rhinitis patients were randomized into 2 groups: control group (CON; n = 14) and yoga group (YOG; n = 13). The control group had normal life and the yoga group was required to complete protocol with yoga training for 60 minutes per session, 3 times per week for 8 weeks.

Results: After 8 weeks, nasal blood flow and nasal congestion were significantly lower than pre-test and CON group ($P < 0.05$). In addition, peak nasal inspiratory flow was significantly higher than pre-test and CON group.

Conclusion: The present findings demonstrated that 8 weeks of yoga training had beneficial effects in allergic rhinitis by decreasing nasal blood flow and symptoms in patients with allergic rhinitis.

TP0676 | Effect of postoperative xylitol nasal irrigation on patients with sinonasal diseases

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Background: To examine the effect of xylitol nasal irrigation in a large sample size of patients who had undergone nasal surgery.

Method: The study included 100 patients with sinonasal disease who underwent endoscopic sinus surgery (ESS), septoplasty, or both concurrently. To identify patients with allergic sensitization, serum-specific immunoglobulin E levels were measured. Nasal symptoms were evaluated with the NOSE (Nasal Obstruction Symptoms Evaluation) and SNOT-20 (Sino-Nasal Outcome Test-20) and via visual analog scale (VAS) scores.

Results: In the ESS group (n = 34), the general nasal symptom score evaluated by the SNOT-20 showed significantly greater improvement in the xylitol group versus the saline group ($P = 0.022$). VAS symptom scores for sneezing ($P = 0.003$), headache ($P = 0.02$), and facial pain ($P = 0.037$) were also more improved in the xylitol group. In the septoplasty group (n = 39), the VAS score for nasal stuffiness showed a significantly greater improvement in the xylitol group when compared with the saline irrigation group ($P = 0.001$). Among the patients with allergic sensitization (n = 31), rhinorrhea symptoms improved significantly more in the xylitol group than in the saline group ($P = 0.024$). The preference survey showed that more than half of the patients in each surgical group preferred xylitol irrigation.

Conclusion: We found that xylitol nasal irrigation was useful in postoperative ESS and septoplasty care. For patients with allergic sensitization, rhinorrhea showed greater improvement in the xylitol group than in the saline group.

TP0678 | Blood eosinophil may predict radiographic sinus opacification in patients with chronic rhinitis

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Background: The association between chronic rhinosinusitis (CRS) and chronic rhinitis remains unclear. The aim of this study is to estimate the predictive factor for sinus opacification in chronic rhinitis patients without obvious CRS.

Method: We retrospectively studied a total of 332 adult patients who visited our clinic from January 2015 to December 2017 with chronic rhinitis. All of the patients underwent endoscopic examination, allergy test, and osteomeatal unit computed tomography. The subjects were assigned to normal sinus (NS) group (Lund-Mackay score [LMS] < 5) and sinus opacification (SO) group (LMS ≥ 5).

Results: A total of 288 patients were eligible for this study. Of them, 183 (63.5%) were classified in the NS group and 105 (36.5%) were SO. Total IgE level and peripheral blood eosinophil count were significantly elevated in SO than NS group ($P = 0.031$ and $P < 0.0001$, respectively). Pearson correlation coefficients were determined that eosinophil count had a positive correlation with the LMS ($r = 0.282$). In the logistic analysis, the interquartile range (0.19×10^9/L) increase of the eosinophil count was significantly associated with SO (OR = 1.76, 95% CI = 1.30-2.39). After adjusted for age, gender, smoking, drinking, and underlying disease, the interquartile range increase of the eosinophil count increased the odds of SO to 1.69 times with statistical significance ($P = 0.007$, 95% CI = 1.17-2.43).

Conclusion: Peripheral blood eosinophil count is an independent predictor of CRS in patients with chronic rhinitis.

TP0679 | Endoscopic sinus surgery under navigation system. Analysis report of 40 cases with chronic polypoid rhinosinusitis

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Background: The aim of this study is to proof the clinical efficiency by using a modern navigation system for Functional Endoscopic Sinus Surgery (FESS).

Method: An optical navigation system was used in clinical routine of 40 patients. Two groups with 20 patients each were examined. Group A was treated with navigation assistance (Karl Storz Navigation Panel Unit NPU), Group B was treated without navigation by conventional FESS. Examination period was limited to 12 months. Median follow-up is 22 and 26 weeks.

Perioperative, intraoperative and postoperative parameters were recorded by workflow-analysis, clinical and radiological findings and standardized questionnaire.

Results: Application of the navigation system needs 1.1 min additional perioperative time in average. Intraoperative time reduction by the navigation system was about 10 min per case (Group A 32.6 (SD 11.2) min, Group B 42.7 (SD 9.5) min). Specific information by the navigation system was evaluated in all surgical areas as useful and additional to a-priori-knowledge. Postoperatively patients from group A (10/89) show lower rate of polyposis then in group B (24/71). Fenestration of the sphenoid sinus were sufficient by CT-evaluation in 100% (group A) and 23% (group B).

Conclusion: The advantages of the examined navigation system in comparison to the gold standard of FESS are proven. Navigation assistance led to an reduced intraoperative time consumption, increased postoperative results and lowered the workload of the surgeons.

TP0680 | Initial clinical Results evaluating the safety and efficacy of olfactory mucosa-derived mesenchymal stem cell therapy as adjunctive treatment for chronic laryngeal and/or tracheal stenosis

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Background: Chronic laryngeal and/or tracheal stenosis (CLTS) could develop after trauma, prolonged assisted ventilation or as a disease complication. Formation of granulation and fibrous tissue results in airway constriction. Patients with CLTS undergo routine surgery every 2-6 months often for years. There is no cure for CLTS. This study evaluates whether additional transplantation of olfactory mucosa-derived mesenchymal stem cells (OM-MSCs) could be safe and improve outcomes of standard therapy.

Method: This Phase 1-2 clinical study (ClinicalTrials.gov ID NCT03130374) was performed at The Republican Research and Practical Center for Otolaryngology with the approval of Bioethical Committee. Patients (n = 7) who were selected for the study gave informed consent. Major exclusion criteria were pregnancy, drug/alcohol addiction, and acute exacerbation of chronic disease. MSCs were obtained from tissue biopsy of olfactory mucosa using the explant method. The biomass of autologous MSCs in 10% human albumin solution was injected submucosally after removal of granuloma and fibrous tissue during surgical intervention. Treatment with autologous MSCs was administered at a dose of 2×10^7 cells/1-2 cm^2 zone of de-epithelialization.

Results: The biomass of OM-MSCs (CD90 + CD105 + CD73 + / CD31-CD45-) was successfully obtained from all the patients. No serious adverse effects were observed after the cell therapy, including fever, allergy, systemic immunosuppression. In all the cases epithelia of the upper airway was restored within 2-6 weeks and the patients were able to have tracheoplasty. No granuloma or scar formation, narrowing of the lumen of the airway or any other symptoms of restenosis occurred within 2 to 15 months after cell therapy. Improvements of both exercise tolerance and health status was seen.

Conclusion: The cell therapy for CLTS using autologous OM-MSCs in combination with standard surgery was safe and well tolerated. OM-MSCs transplantation resulted in the restoration of normal epithelium. Adverse effects including immunosuppression were not observed. Mesenchymal stem cell therapy prevented restenosis in patients with CLTS.

TP0681 | Treatment of paranasal sinus indolent mucormycosis

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Background: Mucormycosis of the nasal cavity and paranasal sinuses is a rare but highly aggressive in patients with diabetes or immunosuppressed patients. However, chronic indolent type of mucormycosis can be observed in immunocompetent patients. In this study, we investigated the clinical and radiological results of indolent mucormycosis of paranasal sinus in healthy patients treated by endoscopic sinus surgery(ESS) alone.

Method: A retrospective review of 9 patients with the diagnosis of indolent mucormycosis of paranasal sinus and treated by ESS alone between 2007 and 2017 was performed. The data were collected from the medical records: age, gender, clinical presentations, pre- and postoperative endoscopic findings, underlying diseases, pathology, pre- and postoperative radiologic findings. Radiologic images were reviewed to assess the involved side and sinus, bony sinus wall changes.

Results: The histopathologic findings showed mucormycosis with broad, non-septated, right-angled hyphae. In spite of diagnosis of mucormycosis, the patients were not any antifungal agents after surgery. There was no progression and recurrence.

Conclusion: In the case of paranasal sinus mucormycosis, endoscopic sinus surgery alone is thought to be sufficient for the treatment for indolent cases in immunocompetent patients without evidence of preoperative CT and endoscopic findings of invasion and antifungal treatment may not be necessary.

TABLE 1 Patient Clinical Characteristics*

Pt no	Age(y)/ gender	Clinical symptoms	With NP	Underlying disease	Involved sinus	F/U(mth)	Recurrence
1	77/F	Facial pain	N	Hypertension	Lt. MS	5	None
2	70/F	Nasal stuffiness, foul odour	Y	Diabetes	Lt. MS	5	None
3	59/F	Facial pain	N	None	Lt. MS	11	None
4	75/F	Facial pain	Y	Hypertension	Lt. MS	13	None
5	48/M	Nasal stuffiness, postnasal drip	Y	None	Rt. MS	8	None
6	68/F	Nasal stuffiness, postnasal drip	Y	None	Rt. MS	12	None
7	67/F	Foul odour, postnasal drip	N	None	Lt. MS	17	None
8	67/F	Foul odour, postnasal drip	N	Diabetes	Lt. MS	10	None
9	60/M	Nasal stuffiness, postnasal drip	Y	None	Lt. MS	24	None

*All patients were treated with endoscopic sinus surgery alone and all survived. Pt no = patient number; y = years; Mth = months; F/U = follow up; F = female; Lt. = left; MS = maxillary sinus; M = male; Rt. = right;' NP = nasal polyp

TP0682 | Postoperative improvement of headache in chronic rhinosinusitis

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Background: According to American ENT head and neck society's diagnostic criteria for sinusitis, headache is a minor symptom of sinusitis. But many patients with chronic headache visited neurosurgery outpatients department, they were diagnosed with chronic rhinosinusitis. They had few nasal symptoms. Among them, many patients had significant improvement on headache after medical or surgical treatment of sinusitis.

Method: he authors reported the improvement of headache after medical or endoscopic sinus surgery, in patients with chronic headache and incidentally founded sinusitis with brain magnetic resonance imaging, and then referred to ENT department. We analysed the duration of headache, headache site, nasal symptoms, headache improvement time after medical or surgical treatment and association with sinusitis lesion site.

Results: A paper reported that sinus headache is only 35% of all headache according to existing diagnostic criteria for sinus headache. But we experienced and would to report better improvement in symptoms of headache after proper management of sinusitis,with literature analysis.

Conclusion: We could improve headache symptoms by proper treatment of sinusitis with selected cases.

TP0684 | The effect of endoscopic sinus surgery and/or medical treatment in patients with aspirin-exacerbated respiratory disease

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Case report: Background and Objection: Aspirin-exacerbated respiratory disease (AERD), so called non-steroidal anti-inflammatory drugs(NSAID) exacerbated respiratory disease, is characterized by nasal polyps, asthma and NSAIDs induced acute hypersensitivity of respiratory tract. It is known to be resistant to surgical removal of nasal polyp and treatment such as intranasal corticosteroid, antibiotics and antihistamine. and the recurrence rate is higher than that of patients without AERD. We evaluated the effect of endoscopic sinus surgery and medical treatment in patient with AERD

Subjects and Method: In our study, We selected four patients with AERD through retrospective chart review. Patients have undergone Endoscopic sinus surgery and postoperative medical treatment. We compared preoperative & postoperative symptom, endoscopic finding of nasal cavity and researched the period using drugs such as antibiotics, antihistamine, intranasal corticosteroid after operation. The period of Postoperative follow-up examination was at least three month.

Results: All patients reported relief of symptoms after surgery compare to preoperative conditions(nasal obstruction, post nasal drip, rhinorrhea) and there was no recurrence of nasal polyp and chronic rhinosinusitis. The average of period of postoperative medical therapy was two months.

Conclusion: Endoscopic sinus surgery and postoperative medical treatment for AERD patients can be effective strategy. In considering therapeutic methods of patient with AERD, Surgery is an effective option of treatment.

SUNDAY, 2 JUNE 2019
TPS 05
PATHOPHYSIOLOGY OF RHINITIS AND CONJUNCTIVITY

TP0685 | Polymorphism in a tight junction gene CLDN10 confers susceptibility to allergic rhinitis

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Background: AR was introduced by allergen exposure, and an immunoglobulin E (IgE)-mediated inflammation of the membranes lining the nose. The claudin protein family is one of the three transmembrane protein components of the tight junction proteins which are major contribution to allergic rhinitis(AR). The claudin-10 (*CLDN10)* gene, encoding a member of the claudin family, is directly or indirectly involved in the cytoskeletal and cell signaling that controls proliferation, differentiation, and other cellular functions in rhinitis diseases. Our study aimed to compare specific IgE levels in serum of allergic rhinitis patients and healthy controls and assess whether polymorphisms in CLDN10 increase the risk of AR.

Method: We tried to verify the hypothesis that *CLDN10* participate in the pathogenesis of allergic rhinitis (AR) through enrolling data from 405 AR patients and 421 controls to investigate the association between *CLDN10* polymorphisms and AR in the Han Chinese population. The six common single nucleotide polymorphisms (SNPs, including rs9302081, rs4773917, rs9302082, rs1467648, rs7995795 and rs1325774) on *CLDN10* were genotyped.

Results: We tried to verify the hypothesis that *CLDN10* participate in the pathogenesis of allergic rhinitis (AR) through enrolling data from 405 AR patients and 421 controls to investigate the association between *CLDN10* polymorphisms and AR in the Han Chinese population. The six common single nucleotide polymorphisms (SNPs, including rs9302081, rs4773917, rs9302082, rs1467648, rs7995795 and rs1325774) on *CLDN10* were genotyped.

Conclusion: In conclusion, our data showed that rs1325774 on ***CLDN10*** was significantly associated with AR, and allele A of rs1325774 might be a genetic risk factor for AR in the Han Chinese population. However, further studies with larger sample sizes and functional studies in animal model are needed to confirm the association.

TABLE 1. Association of ***CLDN10*** polymorphisms with AR under different genetic models.

SNP	Models	Genotype	OR(95%CI)	*P*
rs930281	Addictive	TT vsGT vs GG	1.513 (0.322-7.751)	0.053
	Dominant	(GT+TT) vs GG	1.451 (1.012-2.080)	0.043*
	Recessive	TT vs (GT+GG)	1.469 (0.300-7.202)	0.635
rs4773917	Addictive	CC vsTC vs TT	1.282 (0.805-1.833)	0.614
	Dominant	(TC+CC) vs TT	1.305 (0.942-1.807)	0.110
	Recessive	CC vs (TC+TT)	1.003 (0.710-1.418)	0.985
rs9302082	Addictive	GG vsGA vs AA	0.956 (0.422-1.577)	0.692
	Dominant	(GA+GG) vs AA	1.082 (0.805-1.453)	0.602
	Recessive	GG vs (GA+AA)	0.710 (0.403-1.253)	0.237
rs1467648	Addictive	CC vs CT vs TT	0.749 (0.795-1.475)	0.207
	Dominant	(CT+CC) vs TT	0.965 (0.717-1.299)	0.816
	Recessive	CC vs (CT+TT)	0.401 (0.197-0.818)	0.012*
rs7995795	Addictive	CC vs CT vs TT	0.897 (0.520-1.340)	0.247
	Dominant	(CT+CC) vs TT	0.938 (0.696-1.264)	0.675
	Recessive	CC vs (CT+TT)	0.825 (0.546-1.245)	0.359
rs1325774	Addictive	CC vsCA vs AA	2.267 (0.552-16.461)	0.011 *
	Dominant	(CA+CC) vs AA	1.558 (1.091-2.226)	0.015 *
	Recessive	CC vs (CA+AA)	2.755 (0.506-15.008)	0.241

OR, odds ratio; CI, confidence interval; SNP, single nucleotide polymorphism.
* $P < 0.05$ is provided in bold to emphasize its significance.

TP0686 | Proprotein convertase PACE4 modulates basal progenitor cell fate in IL-4-stimulated human nasal epithelial cells

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Background: Repeated chronic exposure to environmental stressors leads to deleterious hyperplastic, metaplastic, and inflammatory epithelial lesions found in chronic airway diseases. Interestingly, the proteolytic maturation of many secretory proteins involved in airway remodeling is controlled by proprotein convertases (PCs). To date, seven different PCs (furin, PACE4, PC1/3, PC2, PC4, PC5/6, and PC7) have been identified in mammals. We previously found that two PCs, furin and PACE4, are expressed in human nasal epithelial cells. The aim of this study is to investigate if PACE4 can modulate basal progenitor cell fate in primary differentiated HNECs stimulated with interleukin (IL)-4, a central mediator of allergic airway diseases.
Method: Human nasal epithelial cells (HNECs) were isolated from nasal polyps and cultured in an air-liquid interface (ALI) allowing cell differentiation after 14 days. The differentiated HNECs were treated with IL-4. The expression of PACE4 and MUC5AC were assessed by RT-qPCR, western blot analysis, and immunofluorescence staining.
Results: IL-4 treatment increased the expression of PACE4 as well as MUC5AC in HNECs. Immunofluorescence imaging revealed that PACE4 was colocalized with MUC5AC in IL-4-stimulated HNECs. In addition, specific lentiviral shRNA-mediated knockdown of PACE4 significantly reduced MUC5AC expression in IL-4-stimulated HNECs. Furthermore, PACE4 expression was up-regulated in nasal mucosa of allergic rhinitis as compared to those from healthy controls.
Conclusion: These findings collectively suggest that PACE4 plays a role during the differentiation of basal progenitor cell into secretory cell lineage and so may contribute to the progression of Th2-driven airway inflammatory diseases associated with mucous cell hyperplasia and mucus overproduction.

TP0690 | Eosinophil chemokines and clara cell protein 16 production in nasal mucosa of patients with perennial allergic rhinitis

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Background: Eotaxin-2 and RANTES (regulated on activation normal T cell expressed and secreted) are involved in the eosinophil trafficking in nasal mucosa of patients with chronic eosinophilic nasal inflammations, including perennial allergic rhinitis (PAR). Clara cell protein 16 (CC16) is an antiinflammatory protein mainly produced by the secretory epithelial non-ciliated Clara cells. The aim of this study was to investigate the production of CC16 and chemokines eotaxin-2 and RANTES in the nasal mucosa of patients with PAR, before and after intranasal corticosteroid treatment.
Method: Twenty one PAR patients and 20 healthy participants were included in this prospective, cross-sectional study. The concentrations of CC16, eotaxin-2 and RANTES were measured in nasal secretions. PAR patients administered fluticasone furoate nasal spray (220 μg daily for 14 days). We performed nasal cytology, symptom score assessment and inflammatory mediator detection prior and after the therapy.
Results: The level of CC16 in patients with PAR was lower than in the healthy subjects (P = 0.023). The eosinophil counts and local concentrations of eotaxin-2 and RANTES were higher in patients with PAR in comparison with controls (P = 0.008, P = 0.001, P = 0.031, respectively). We also found a negative correlation between the CC16 and eotaxin-2 levels in nasal secretions of PAR patients (r = -0.492, P = 0.023). After corticosteroid therapy, the patients with PAR had lower nasal symptoms, eosinophil counts, eotaxin-2 and RANTES levels and higher levels of CC16 (P < 0.001 for all parameters).
Conclusion: Our results suggest the presence of a negative correlation in production of CC16 and eotaxin-2 in nasal mucosa of patients with PAR. Intranasal corticosteroids have a suppressive effect on mucosal eosinophilic inflammation and a stimulating effect on local CC16 production.

TP0692 | CD48 in intermittent allergic rhinitis

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Background: In the pathogenesis of allergic diseases including intermittent allergic rhinitis (IAR), the inflammatory reaction is of importance. CD48 antigen expression increases in inflammatory conditions and in eosinophilia. The purpose of the study was to assess the concentration of soluble form of CD48 (sCD48) in serum of patients with intermittent allergic rhinitis, try to find correlations with eosinophil — related parameters and diseases activity and to compare to healthy controls.
Method: In all patients details medical history, assessment of peripheral blood eosinophilia, skin pricks test with inhalant allergen extract, fractional exhaled nitric oxide (FeNO) — bronchial and nasal fractions, sCD48, ECP and eotaxin serum concentration were estimated. Serum samples and FeNO were collected once in control group and twice in the rhinitis group: in the asymptomatic period and in the phase of exacerbation of symptoms during pollen season. The severity of symptoms was assessed using the Total Nasal Symptom Score (TNSS). 25 (14 women, 56%, mean age 28, 23-39 years) patients with allergic intermittent rhinitis in exacerbation phase and 11 (8 women, 72%, mean age 29, 23-35 years) out of the season and 26

controls (18 women, 69%, mean age 38, 26-60 years) were included into the study.

Results: sCD48 level and FeNO nasal fractions were significantly higher in patients with IAR in exacerbation phase than out-of the season ($P < 0.05$). Differences in ECP, eotaxin serum levels and bronchial fraction of FeNO were not significant between season and out of the season. FeNO nasal and bronchial fractions levels were significantly higher in patients with IAR in exacerbation phase than in controls ($P < 0.05$). ECP and eotaxin serum levels in exacerbation phase were higher than control group although nonsignificant.

Significant positive correlation was observed between sCD48 and in allergic rhinitis the exacerbation phase and between sCD48 and TNSS (last two weeks) in the remission phase. Other significant correlations also were observed between FeNO bronchial fraction and, TNSS (last 12 hours) and ECP in remission phase.

Conclusion: sCD48 may be a biomarker to exacerbation phase in patients with IAR. FeNO nasal fractions may be useful in the assessment of exacerbation. Correlation between sCD48 and number of blood eosinophils confirms the importance of CD48 as the effector unit of allergy.

TP0693 | Evaluation of PD-1 expression on different subsets of T-lymphocytes in donors and patients with allergic rhinitis and bronchial asthma

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Background: The pathogenesis of allergy includes increasing of activated cells number or decreasing of number of cells with suppressive activity. Thus, the investigation of markers of activation and suppression such as PD-1 and CD25 on T-lymphocytes in patients with allergic diseases can be interesting. Earlier, we have demonstrated that the population of $CD4^+CD25^{hi}$ cells associated with the T-regulatory cells had higher expression of PD-1 in donors than in patients with allergic rhinitis (AR). The number of $PD\text{-}1^+$ cells, which can regulate negatively the immune response, increased after allergen-specific immunotherapy. Herein, we report the study of the expression of these markers in patients with different types of sensitization and patients with AR and bronchial asthma (BA).

Method: There were groups of healthy donors (n = 10, age 21.5 (20; 35), group I), patients with AR with pollen sensitization (n = 11, age 31 (19; 39), group II) and patients with AR with polyvalent (indoor and out-door aeroallergens) sensitization (n = 9, age 34 (20; 46), group III). All types of sensitization were confirmed by skin prick tests. We have also analyzed the groups of patients with AR without BA (n = 14, age 35 (19; 52), group IV) and AR with BA (n = 6, age 27 (20; 46), group V). PBMCs were extracted from heparinized blood and prepared for flow cytometry. Statistical analysis was made by using Mann-Whitney criterion, the difference was considered significant if $P < 0.05$.

Results: We have found the significantly lower level of $CD4^+CD25^{hi}PD\text{-}1^+$-lymphocytes in patients groups (II and III) comparing with donors. There was also increasing of $CD8^+$-cells level in the group of patients with pollen sensitization (I vs II). In the same time, we didn`t find any significant difference between both patients' groups (II vs III).

Patients with AR without BA had lower amount of cells of $CD4^+CD25^{hi}$, $CD4^+CD25^{hi}PD\text{-}1^+$, $CD8^+CD25^+PD\text{-}1^+$ subsets and increasing of $CD8^+$, $CD8^+CD25^+$ cells comparing with donors. The level of $CD4^+CD25^+$ and $CD4^+CD25^{hi}$ cells was decreased in patients with AR+BA. Patients with AR+BA had increased level of $CD4^+CD25^{hi}PD\text{-}1^+$ cells in comparison with patients without BA.

Conclusion: Our results confirm the hypothesis that the pathogenesis of allergic diseases can be associated with the imbalance of the processes of cell activation and suppression. The data also demonstrate the differences of the immune response development between patients with different types of sensitization.

TP0694 | Evaluation of basophil response in dual allergic rhinitis patients

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Background: Allergic rhinitis (AR) and local allergic rhinitis (LAR) are well defined rhinitis phenotypes. Nevertheless, some rhinitis patients with positive skin prick test (SPT) and nasal allergen challenge (NAC) to seasonal allergens, also display positive NAC to perennial allergens whereas they test negative in SPT. We propose the term dual allergic rhinitis (DAR) for this new phenotype. The goal of this study was to evaluate the basophil response to seasonal and perennial allergens in DAR subjects.

Method: 10 DAR patients, defined as perennial symptoms, SPT/NAC+ with olive tree or grass pollen and SPT-/NAC+ with *Alternaria alternata* or *Dermatophagoides pteronyssinus*, were recruited. 6 NAR individuals (SPT/NAC- with relevant allergens in our area) and 10 AR subjects (SPT/NAC+ with olive pollen and seasonal symptoms) were included as controls. Two separated NACs with the seasonal and perennial allergens were performed in DAR and NAR patients, and basophil activation tests (BAT) with both seasonal and perennial allergens (1-0.0001 ng/mL) were carried out before and after each NAC. Serum specific IgE (sIgE) was measured at baseline in all study groups.

Results: : All AR and DAR patients had positive NAC responses, whereas the NAR individuals did not. At baseline serum sIgE to the

seasonal allergens was lower in DAR patients (1.18 kU/L), than in AR subjects (12.9 kU/L). Conversely, BAT reactivity (%CD63) was similar in both DAR and AR groups (60.1 and 54.7, respectively). All NAR subjects tested negative in BAT with both seasonal and perennial allergens. All DAR patients tested positive in BAT with the seasonal allergen, and 60% tested positive with the perennial allergen. In DAR subjects, CD63 expression in BAT showed significant differences between seasonal and perennial allergens from 1 to 0.01 ng/mL concentrations. In both DAR and NAR patients, the NACs did not induce significant changes in basophil reactivity with either seasonal or perennial allergens. Regarding sensitivity (measured by CD-Sens) there was observed an increase after NACs that was significant for the seasonal allergens.

Conclusion: For the systemic sensitization, DAR individuals display similar basophil reactivity but lower serum sIgE compared to AR patients. The basophil reactivity for the local sensitization in DAR subjects is similar to that reported for LAR patients in previous studies. The NAC does not affect basophil reactivity but increase their sensitivity.

TP0696 | The effects of myeloid and plasmacytoid dendritic cells on group 2 innate lymphoid cells in allergic rhinitis patients

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Background: Group 2 innate lymphoid cells (ILC2s) were recently reported to serve a critical role in allergic diseases. Myeloid dendritic cells (mDCs) and plasmacytoid DCs (pDCs) play significant roles in promoting and suppressing the allergic immune response respectively. However, the effects of DCs on ILC2s in allergic diseases especially for allergic rhinitis (AR) patients remain unclear. We sought to address the roles of mDCs and pDCs in regulating ILC2 function in AR.

Method: The presence of ILC2s, mDCs and pDCs were measured using immunofluorescence in the nasal mucosa of AR patients. mDCs and pDCs were co-cultured with human PBMCs or ILC2s from AR patients or healthy subjects. The cytokines in the supernatant, the intracellular cytokines, transcription factors and signaling pathways were evaluated using ELISA or flow cytometry, and the following mechanisms were further investigated. The levels of peripheral ST2 + mDCs or ST2 + pDCs were studied in AR patients with inhaled allergen challenge.

Results: We identified that mDCs activated ILC2s from AR patients to produce Th2 cytokines and increased the levels of GATA-3 and STAT signaling pathways, in which IL-33-producing mDCs exerted the major role. pDCs inhibited the cytokines production of ILC2s from AR patients by secretion of IL-6. We further identified the high levels of ST2 (IL-33 receptor)$^{+}$mDCs and ST2^{+}pDCs in the blood of AR patients under the antigen inhalation.

Conclusion: mDCs promote ILC2 function via IL-33/ST2 pathway and activation of pDCs suppress ILC2 function via IL-6 in AR patients. Our findings offer a novel understanding about the interplay between DCs and ILC2s in the pathology of allergic diseases.

TP0697 | Dysregulated coagulation cascade and fibrinolysis system lead to fibrin deposition in allergic rhinitis

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Background: Dysregulation of the coagulation cascade and fibrinolysis system may play an etiologic role in many diseases. Allergic diseases such as bronchial asthma, atopic dermatitis, and conjunctivitis are also associated with fibrin accumulation caused by a change in hemostasis. However, only a few studies have dealt with the relationship between allergic rhinitis (AR) and the coagulation system. We investigated the difference of coagulation and fibrinolysis cascade components between an AR mouse model and a control mice.

Method: BALB/c mice were sensitized and challenged with ovalbumin. Multiple parameters of coagulation cascade and fibrinolysis system such as Factor II, V, VII, X, and XIII; tissue-type plasminogen activator (t-PA); urokinase-type plasminogen activator (u-PA); plasminogen activator inhibitor-1 (PAI-1); and fibrin were compared between the allergic rhinitis model group and the control group.

Results: The symptom scores and eosinophil counts were higher in the AR group than in the control group ($P < 0.01$). The mRNA expression level of u-PA ($P = 0.040$) was significantly lower, and the expression levels of Factor II ($p = 0.038$) and Factor X ($p = 0.036$) were significantly higher, in the AR group. Immunohistochemical staining revealed that most of the fibrinolysis system and coagulation cascade components were localized to the epithelium, endothelium, and submucosal glands of the nasal mucosa. u-PA was downregulated in the AR group, whereas fibrin deposition was more prominent in the AR group than in the control group.

Conclusion: In AR, particular components of the coagulation cascade were increased and fibrinolysis system were decreased compared to normal control. This difference may be associated with the fibrin deposition in the mucosa of AR mouse model.

TP0698 | LncRNA FR215775 regulates Th2 differentiation through Cav1.3 pathway in AR murine

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Background: To identify the effect of lncRNA FR215775 in CD4 + T cells on the murine models of allergic rhinitis (AR).

Method: The microarray was conducted to identify the expression profiles of lncRNA in CD4 + T cells in AR murine. Bioinformatic analysis were used to show related pathways of T cell differentiation. qRT-PCR was performed to determine the lncRNA FR215775 expression in primary Th2 cells and Sh-FR215775-Ads was conducted to perform cck-8, CBA, FACS in order to determine the functions of FR215775 in vitro. In vivo transfected cells or not were intravenously injected into AR mice. HE staining, AB-PAS staining, TBO staining were performed and the levels of IL-2, IL-4, IL-5, IL-6, IL-10, IL-17A, IFN-γ and TNF were detected by CBA kit.

Results: A total of 158 deregulated lncRNAs were detected and calcium-signaling pathways may be involved in the development of T cells in AR pathology. The expression of FR215775 was specific higher in murine primary Th2 cells. After knocking down FR215775, CD4 + T cell proliferation was inhibited,the expression of IL-4, IL-5 in cell culture supernatant were significantly decreased as well as the percentage of Th2 cells ($P < 0.001$, $P < 0.05$). Moreover, the relative expression of cacna2d was significantly decreased while prckg mRNA was significantly higher($P < 0.001$, $P < 0.0001$). The Sh-FR215775-Ads AR group showed less serious allergic symptoms and low level of OVA-specific IgE($P < 0.01$).Meanwhile, this group attenuated the allergic inflammation, including the decrease of eosinophilia inflammation, goblet cell hyperplasia, and mast cell inflammation in the nasal mucosa. what's more, the down-regulation of Th2 cytokines IL-4,IL-5 were showed in the serum and NALF of this group($P < 0.01$).

Conclusion: The present study showed the differential expression profiles of lncRNAs in the CD4 + T cells of an AR murine model. FR215775 may play a significant role in the function and differentiation of Th2 cells through Cav1.3 pathway and it may encourage allergic inflammation. These results may provide significant insights into AR pathogenesis and offer new treatment targets to alleviate it.

TP0699 | Involvement of galanin and galanin receptor 2 in a mouse model of allergic rhinitis

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Background: Galanin (GAL) is a neuropeptide that regulates inflammatory processes, and that is widely expressed in the central and peripheral nervous systems. While such neuropeptides have been implicated in conditions such as arthritis and chemically induced ileitis, their roles in allergic rhinitis (AR) remain unclear.

Method: We herein developed a murine model of AR that comprised control (Group A), systemic-sensitization (Group B), mild-AR (Group C), and severe-AR (Group D) treatment groups. The *GAL* and *GAL receptor* (*GALR*) mRNA and protein expression levels and localization patterns in each group were examined via a combination of reverse transcription PCR, western blot, and immunohistochemical analyses. The effects of administering a GALR2 antagonist (M871) to mice with severe AR were also evaluated.

Results: *GAL* and *GALR2* were expressed in nasal mucosa and brain (control) samples collected from both control and AR mice. Likewise, GAL and GALR2 were expressed at similar levels, and were both localized to ciliated epithelial and submucosal gland cells of the nasal mucosa, in all four treatment groups. Notably, intranasal administration of M871 significantly reduced the incidence of nose-rubbing behaviors and sneezing in severe-AR compared to control mice.

Conclusion: Our data suggest that GAL signaling may not change progressively with increasing nasal sensitization; thus, it may exacerbate rather than directly trigger AR. Nevertheless, our findings suggest that GAL-GALR2 signaling likely mediates AR development, and thus supports that its inhibition may be a novel therapeutic strategy for AR.

TP0700 | IL-9 expression in ocular allergy

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Background: IL-9 is known to act as a pro-inflammatory cytokine and is associated with the immunopathogenesis of allergic diseases including asthma. We aimed here to determine whether IL-9 is contributing to ocular allergy inflammation by immunophenotyping human conjunctival tissues, an *in vivo* OVA model of experimental conjunctivitis (EIC) and *in vitro* mast cells. We investigated the human conjunctival tissue expression of IL-9, and the effect of IL-9 on cytokine secretion profiles in mouse bone marrow-derived mast cells.

Method: Archived human conjunctival tissue biopsies collected from seasonal allergic conjunctivitis and non-allergic donors were stained for IL-9, IL-9R and mast cell markers (tryptase, c-kit). The function of IL-9 was also studied *in vitro*, using bone marrow-derived mouse mast cells, where the cells were exposed to ionomycin or IgE in the presence of neutralising anti-IL9, anti-IL9R Abs or using RNAi technology to inhibit IL-9 pathways. Cytokine secretion was assayed by multiplex bead arrays at different time points (15 and 60 min and 24, 48, 72 hrs).

Results: We found that IL-9 expression within human conjunctival tissues was upregulated during 24 hr post allergen challenge and was expressed by mast cells and Th9 cells. *In vitro* studies revealed that inhibition of IL-9R led to decreases in IL-4, IL-5 and IL-9 secretion from bone marrow-derived mouse mast cells ($P < 0.001$, $P < 0.05$, $P < 0.05$ respectively) whereas IL-10 secretion was not affected. The data from the EIC model also revealed a high level expression of IL-9 in inflamed areas where mast cells expressed IL-9R.

Conclusion: In conclusion, IL-9 pathways are involved in ocular allergy responses.

TP0701 | IgE ratio in tears: A predictive tool of ocular allergic inflammation

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Background: In the context of ocular allergy, various immunological profiles were associated with different clinical phenotypes, but none was able to elicit a specific biological marker allowing a fast differential diagnosis between the severe sight-threatening and mild forms. In this study we wanted to demonstrate the tear IgE (measured/exuded) ratio as a useful biological marker of ocular sensitization independently of the clinical phenotype, in order to distinguish severe inflammatory status from less severe forms.

Method: Tear samples and sera from 78 ocular allergy patients and 19 control subjects, were analyzed. Total IgE and albumin were measured for calculating the tear IgE ratio defining two subgroups of samples, (i) the R ≥ 4-subgroup, corresponding to a local IgE production and (ii) the R < 4-subgroup. Based on this classification, eosinophil cationic protein, Th1 and Th2 cytokines (IFN-g, IL-4, -5, -6, -8 and -10) in tears were analyzed, using respectively fluoroenzyme immunoassay and multiplex bead analysis. Protein electrophoretic profiles were investigated using tear capillary electrophoresis.

Results: The R < 4-subgroup gathered the biological criteria corresponding to an inflammatory process compared to the R ≥ 4-subgroup, with higher levels of tear albumin, eosinophil cationic protein, and Th1 and Th2 cytokines. Moreover, immunoglobulin light chains, zinc-α 2-glycoprotein and lysozyme-C were significantly modulated in the R < 4-subgroup. Lactoferrin was only modulated in the R ≥ 4-subgroup compared to the control group.

Conclusion: This study showed that an IgE ratio lower than 4 is associated with increased levels of Th1/Th2 cytokines and eosinophil cationic protein and with a particular tear protein profile, and that it must be carefully interpreted as a warning sign of a severe inflammatory context.

TP0702 | Nasal provocation test and evaluation of the predictive instruments for the diagnosis of local allergic rhinitis

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Background: Rhinitis affects around twenty percent of the population around the world, and a phenotype of rhinitis that has not yet been studied is local allergic rhinitis (LAR), which gold standard test for diagnosis is the nasal provocation test (NPT). The objective of this study is to describe the results of the NPT of patients with suspected LAR and compared the instruments used in the evaluation.

Method: A cross-sectional study, including patients 18 to 75 years old, from January to March 2018, with clinic and history of allergic rhinitis, with negative skin test and negative specific IgE to mite. Patients underwent NPT with standardized extract of Dermatophagoides pteronyssinus in increasing concentrations, and considered positive when the Scale of Symptoms score was greater than or equal to 5. Inspiratory Peak Flow (IPF) was considered not normal when its variation was greater than or equal to 30%, and the Visual Analogue Scale (VAS) greater than or equal to 5 points. Eosinophil counts and total serum IgE were analyzed in the peripheral blood.

Results: Twenty-eight patients were included, 75% were women, mean age was 50 ± 15.44 years. The NPT was positive in 42%, all in the concentration of 1/10 and there was no reaction to the saline solution. The mean duration of the disease, family history of rhinitis and rhinitis severity, did not show significant differences. Mean values of VAS and IPF variation (31.33 ± 6.97 l/min) were significant (P = 0.00). Mean values of eosinophils and serum IgE did not show significant differences. In a multivariate model, we observed that symptoms scale (P = 0.017), IPF (P = 0.008), and VAS (P = 0.04) were associated significantly with positive NPT, and the better explanatory model included the Scale of symptoms. The final VAS and the final PFI, in a linear model, were significantly associated with higher symptom scale.

Conclusion: The symptom scale was the best outcome for the evaluation of the NPT, but VAS and IPF also appear to be useful as predictors of NPT positivity.

TP0703 | Correlation between nasal provocation test, skin reactivity and specific IgE to dermatophagoides pteronyssinus and lepidoglyphus destructor

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Background: Current diagnosis of mite allergy relies on the evaluation of the papular diameter of skin prick test (SPT) and/or specific IgE. Nevertheless, other parameters of skin test may be considered, namely the minimum allergen concentration that elicits a papule. The aim of this work was to study how skin prick tests (papular maximum diameter and minimum allergen concentration that elicits a positive test) and specific IgE can predict the nasal provocation outcome.

Method: Thirty-eight patients with rhinitis and history of mite allergy were selected. SPT (Diater® extracts) to *Dermatophagoides pteronyssinus* (Dp) and *Lepidoglyphus destructor* (Ld) were performed

using 5, 0.5, 0.05 and 0.005 HEP/mL concentrations. Specific IgE to Dp and Ld were also measured. Nasal provocation tests (NPT) (Diater® extracts) carried out to Dp and/or Lp.

Positivity criteria were: SPT papular maximum diameter (pmd) ≥ 3 mm; IgEs ≥ 0.35 kUA/L; NPT with decreased peak nasal inspiratory flow (PNIF) ≥ 40% or 2 criteria of ≥ 5 sneezing, rhinorrhea, decreased PFIN ≥ 20 from basal value.

Results: Twenty-six patients (12 male and 14 female, mean age 31.5 ± 16.6 years) were submitted to NPT to Dp, twelve having a positive test. Regarding these 12 patients the pmd ranged from 5 to 17 mm (mean 8.31), 75% had positive SPT to 0.005 HEP/mL and mean specific IgE was 47.4. In the 14 patients who had negative NPT to Dp the pmd ranged from 0 to 13 mm (mean 5), only 3 having positive SPT to 0.005 HEP/mL; mean specific IgE was 20.2.

Thirty-two patients (17 male and 15 female, mean age 31.2 ± 15.8 years) were submitted to NPT to Ld, twenty-four having a positive teste. In those the pmd ranged from 5 to 30 mm (mean 10.9), 71% had positive SPT to 0.005 HEP/mL; mean specific IgE was 26.5. In the 8 patients who had negative NPT the pmd ranged from 0 to 6 mm (mean 1.1), two had positive SPT none of them to 0.005 HEP/mL; mean specific IgE was 0.1.

Conclusion: Conventional SPT as well has specific IgE showed a high rate of false positivity for Dp considering the NPT results; test with 0.005 HEP/mL may help to assess true positivity. For Ld conventional SPT and specific IgE were good predictors of nasal response.

SUNDAY, 2 JUNE 2019
TPS 06
GENETICS, EPIGENETICS AND MECHANISMS

TP0704 | Homozygous status for CHI3L1 variant is associated with decreased prescribing of inhaled corticosteroids

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Background: Asthma is a chronic respiratory disease, characterised by relapse and remission of symptoms. The CHI3L1 (rs4950928) variant has been associated with diminished risk of asthma-related hospital admissions, as previously reported by Cunningham et al. The association between this variant and asthma-related prescribing and asthma exacerbations over childhood is unclear, as most of the studies are cross-sectional. We tested the hypothesis that individuals with the GG genotype of the CHI3L1 variant are prescribed less asthma medication during childhood and early adulthood.

Method: A secondary analysis of BREATHE, a cross-sectional study of gene-environment associations with asthma severity was undertaken. Data had been collected on participants with asthma, aged 3-22 years, between 2003 and 2005, in Tayside and Fife, Scotland. Through collaboration with the Health Informatics Centre in Dundee, data were linked to longitudinal databases spanning 9 years including Accident & Emergency, community prescribing and Scottish Morbidity Records (hospital admissions). Data were analysed using generalised linear models with random effects for repeated measures.

Results: The analysis was performed on 902 individuals (mean age of 14 in 2005). At the end of the 9-year period, 420 (46.6%) individuals had been prescribed ≥ 1 courses of prednisolone, 682 (75.6%) had been prescribed inhaled corticosteroids, 360 (39.9%) had been prescribed long-acting β_2-agonist combined with corticosteroids and 247 (27.4%) had been prescribed ≥ 1 anti-leukotriene antagonists. Inverse associations were found between individuals with the GG genotype for the CHI3L1 variant and the prescribing of inhaled corticosteroids (GG vs CC — Incidence Rate Ratio (IRR): 0.55, 95% CI: 0.33-0.93; GG vs GC — IRR: 0.54, 95% CI: 0.32-0.92). No association was found between the CHI3L1 variant and asthma-related hospital admissions.

Conclusion: In children and young adults, the homozygous GG is associated with long-term decreased prescribing for inhaled corticosteroids compared to those carrying at least one C allele. Defining subgroups of individuals requiring more medication could help develop targeted management strategies and potentially predict treatment costs.

TP0705 | GSTT1 and GSTM1 polymorphisms in asthma

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Background: The inability of GST variants of the enzymes to detoxify the reactive oxygen species (ROS) contributes to the activation of the inflammatory process, bronchoconstriction, and asthma .An increasing risk for asthmatic disease and an increase in individual susceptibility to pro-allergy effects associated with xenobiotics have been demonstrated to be linked to functional polymorphisms of GST enzymes. *GSTM1* and *GSTT1* null polymorphisms could be associated with the inability of glutathione S-transferases (GSTs) variants of the enzymes to detoxify the reactive oxygen species (ROS) and contribute to a more severe prognosis in asthmatics.

Method: For GSTT1 and GSTM1 we analyzed asthmatics (n = 96) compared with control group (n = 160); the polymorphisms were analyzed by Multiplex-PCR. Control of asthma assessed by ACQ7 and PAQLQ. Statistical analysis was performed with PASW-24 establishing a significance level of $P < 0.05$.

Results: In asthmatics there are 61 females and 35 males; in controls: 93 females and 67 males ($P = 0.468$). The mean age ±SD of the asthmatics was 38.69 ± 20.013 years .The mean age ±SD in the control group was 44.15 ± 12.63 years ($P = 0.019$). In asthmatics genotype frequencies of GSTT1*0 were : 50 (52.1%) and GSTT1 + were : 46 (47.9%); in control group genotype frequencies of GSTT1*0 were : 49 (30.6%) and GSTT1 + were : 111(69.4%). The GSTT1*0 is more frequent among asthmatics ($P = 0.001$). In asthmatics genotype frequencies of GSTM1*0 were : 51(53.1%) and GSTM1 + were : 45(46.9%); in control group genotype frequencies of GSTM1*0 were : 72 (45.0%) and GSTM1 + were : 88(55.0%). There is no statistical differences ($P = 0.258$). The genotype GSTT1*0 confers a risk of being asthmatic of 2.647 times when compared with GSTT1 + genotype and adjusted for age: OR[b]: 2.647 [1.548-4.528]; $P < 0.001$. The genotype GSTT1*0 confers a risk of being allergic asthmatic of 4.863 times when compared with GSTT1 + genotype and adjusted for gender: OR[b]: 4.863 [1.137-20.788]; $P = 0.033$. We constructed a genetic risk score for each participant to have asthma vs controls .The individuals that has a high genetic risk score according to this model have an increased risk of 5.418 [2.344-12.523]; $P < 0.001$ of having asthma comparing to those low genetic risk score.

Conclusion: GSTT1*0 polymorphisms could lead to different genotype specific response to therapy and different endotypes/phenotypes among asthmatic patients.

TP0706 | Sensitivity towards house dust mite induced nasobronchial allergy in relation to TGF-β1 C-509T polymorphism among west bengal population, India

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Background: House Dust Mites (HDMs) play an important role in causing various nasobronchial allergic manifestations around the world. Since the establishment of the role of HDM (Acarinae: Pyroglyphidae) in allergic diseases, many survey on their diversity and distribution have been carried out around the world. The present study has been designed to explore the dust mite fauna in West Bengal, India along with the identification of possible association of candidate gene TGF-β1 with disease manifestation among West Bengal population, India.

Method: House Dust (HD) samples were collected from the patient as well as control houses and analyzed for the presence of dust mites. HD and six constituent mites namely *Dermatophagoides pteronyssinus* (DP), *Dermatophagoides fariane* (DF), *Blomia tropicalis* (BT), *Acarus siro* (AS), *Lepidoglyphus destructor* (LD), *Tyrophagus putrescentiae* (TP) were tested for allergenic potential in 372 patients through Skin Prick Test (SPT) on the basis of their abundance in the West Bengal environment. Total serum Immunoglobulin E (IgE) was measured. Polymerase chain reaction based restriction fragment length polymorphism was done in patients and controls to characterize a functional C-509T polymorphism of TGF-β1. Written informed consents were taken from the participants.

Results: Dust analysis revealed that a total of 51 species of mites belonging to 34 genera and 17 families were identified. HD was the major elicitor exhibiting 92.42% response. DF showed the highest sensitization (87.87%) among the dust mites followed by DP (81.21%) and BT (74.24%). AS, LD, TP showed 33%, 25% and 18% sensitizing potential respectively. Individuals of age group 15-40 were the worst sufferers. SPT grades and total IgE were positively correlated for each of the allergens. The present study revealed no significant difference in allele and the genotype frequencies of the said polymorphism between mite-sensitive patients and non-sensitive controls.

Conclusion: West Bengal is very rich in dust mite fauna and HDM is a common aeroallergen. AS, LD and TP sensitization are first time reported from India and can be recommended for inclusion of routine SPT for better outcome. Further study is required to know the complex interactions of genetic and environmental factors leading to HDM sensitizations.

TP0707 | Association of asthma and lipoprotein cholesterol levels: A two-sample mendelian randomization analysis

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Background: Observational studies and meta-analysis studies indicated the associations between blood lipoprotein cholesterol and asthma. Several clinical intervention studies have demonstrated that PCSK9 and CETP inhibitors could reduce LDL-C levels and increase HDL-C levels. However, there are few studies investigate the effects of PCSK9 and CETP inhibitors on asthma. We aimed to investigate the causal relationship between asthma and serum levels of high-density lipoprotein cholesterol levels and low-density lipoprotein cholesterol levels using PCSK9 and CETP genotypes by Mendelian randomization (MR).

Method: Our analyses were performed using summary statistics from Global Lipids Genetics Consortium (GLGC) and Asian Genetic Epidemiology Network (AGEN). The association between all genetic variants and exposure of interests were calculated using an inverse-variance weighted method. Based on genetic risk score as an instrumental variable, we then conducted two sample MR. Sensitivity analyses were applied to detect pleiotropy using MR-Egger and forest plot analysis.

Results: The primary analysis included 19 439 participants (mean age, 48.4 years; 50.8% women) from the Taiwan Biobank including 2177 asthma patients. The PCSK9 and CETP genetic risk scores were associated with lower levels of LDL-C and higher levels of HDL-C, but none of them shown significant associated with asthma. There were no directional genetic pleiotropy effects in our study.

Conclusion: In observational analyses, HDL-C and LDL-C were associated with asthma. However, our results were not consistent with these associations. The observational studies may be biased by reverse causal association and unmeasured confounding factors. This is the first Mendelian randomization analysis to study the relationship between asthma and lipoprotein cholesterol levels.

TP0708 | A genome-wide association study identify the association between SNP Rs2304053 rs215274 and adult asthmatics with obesity abstract

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Background: In recent years, with the changes in social pattern and eating habits, asthma and obesity have gradually caused public

issues. The simultaneously increasing prevalence of both asthma and obesity was suggested a potential intrinsic link between two chronic diseases. Some studies found that genetic factors played an important role in both chronic diseases. It is necessary to analyze the link between asthma and obesity. A genome-wide analysis study (GWAS) has been conducted to identify genetic variants which are susceptible to asthma and concerned about the effect of the single nucleotide polymorphism on asthma and obesity. And further replicate two novel SNPs in a hospital based case control study.

Method: There were 477 asthmatic and 477 healthy participants respectively and 645918 SNPs for exploring associations from the Taiwan Biobank. Two candidate SNPs (rs2304053 in the FAT2 gene and rs215274 in the SEMA3E gene) would be selected after analyzing by genome-wide association method. In addition, there were 303 asthmatics from Kaohsiung Chang Gung Memorial Hospital and 491 healthy participants from Kaohsiung community would be used to test two candidate SNPs.

Results: SNP rs2304053 and rs215274 were associated with obese asthma by GWAS (P = 9.83*10^{-7}, 2.85*10^{-5} respectively). From replicated results, the BMI of the SNP rs215274 GG genotype was higher than GT/TT genotype in the asthmatics group. However, we did not find association between asthmatics and SNP rs215274 and rs230453 polymorphism.

Conclusion: In the Taiwan Biobank data, we found that two SNPs (rs2304053 and rs215274) are candidate genes on asthmatics with obesity. Both rs2304053 and rs215274 were not different between asthma and control in a hospital based case control study. However, we found that the G allele type in the SNP rs215274 was associated with obesity.

TP0709 | Particulate matter and asthma: Effect modification by tumor necrosis factor-α polymorphisms in lung function

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Background: Exposure to particulate matter induced to oxidative stress and inflammatory mediators in the lower airways and reduced lung function. Variability in lung response to air pollutants exposure has been associated with genetic polymorphisms that modify the inflammatory and immunological responses to the inhalation of these pollutants. To evaluate the effect modification of TNFA-308 inflammatory gene polymorphisms in the association between particulate matter concentrations (PM10) and forced expiratory volume in the first second (FEV1).

Method: Sample of 112 children between 6 and 14 years of age, with medical diagnosis of asthma. Spirometry was performed and buccal cell were collected and used as the source of DNA for genotyping assays. TNFA-308 was genotyped by the polymerase chain reaction technique (Applied Biosystems). Generalized Linear Models have been used, and the relation between PM_{10} and VEF1 has been estimated using Polynomial Distributed Lag Model (PDLM) methods. The effect modification of the genetic polymorphisms has been rated including the genotypes and pollutants in the work model.

TABELA 1 Características da população de estudo

Sex (male) %	62.5
Age (%)	9 ± 2.38
Environmental tobacco smoke (yes)%	32.1
Inhaled corticosteroid use (%)	83.9
Symptoms of asthma in the last four week (%)	32.1
TNF_308 G>A (%) GG	75.9
GA ou AA	24.1
G	87.5
A	12.5
VEF1 (as % predictive ± SD)	85 (14.2)

Results: The frequencies of GG, GA and AA genotypes were 75.9%, 23.2% and 0.9%, respectively. Children with the polymorphic genotype TNF-308 GA or AA had a statistically significant reduction in FEV1 associated with PM10 exposure in lag 0 (-11.23, 95% CI: -19.23, -2.45), lag1 (-5.6, 95% CI: -10.16, -0.8) and in the cumulative 5 days (-9.37, 95% CI: -13.75, -4.76) 308 GG.

Conclusion: This study demonstrated that the genetic polymorphism in the TNFA-308 inflammatory gene increases the susceptibility to the adverse effects of air pollutants on lung function. The identification of subgroups of the population most susceptible to the harmful effects of air pollutants can help to define strategies to reduce the exposure of these individuals to environmental pollution.

TP0711 | Epithelial posttranscriptional gene regulatory networks in chronic airway inflammation: In silico mapping of RNA-binding protein expression

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Background: Altered messenger RNA (mRNA) turnover and translation rates are important mechanisms by which post-transcriptional gene regulation (PTR) contributes to inflammation. RNA-binding proteins (RBPs) chiefly coordinate these processes but their pathogenic role in chronic lung inflammatory diseases is only partially

characterized. We aimed at evaluating the expression of a curated list of mRNA-binding RBPs (mRBPs) [Nature 2014;15:829] in selected transcriptomic GEO databases of primary airway epithelium isolated in lung inflammatory diseases. We hypothesized that global changes in mRBP expression can be used to infer their putative pathogenetic roles and identify novel disease-related regulatory networks.

Method: We evaluated the expression of 692 mRBPs in a microarray database generated from epithelial cells obtained by bronchial brushings of stable COPD patients (C), smokers (S) and non-smokers (NS) as controls with normal lung function (n = 6/12/12 each, respectively) [Cancer Res. 2006;66:10729] deposited in the Gene Expression Omnibus (GEO) repository (GEO ID: GSE5058). Fluorescence intensity data from individual datasets were extracted and normalized by the medians for fold change (FC) expression among groups. FCs were set at ≥ |2.0|0.0 with a false discovery rate (FDR) of ≤ 0.05. Pearson correlation matrices for correlated expression changes and heatmaps were generated using tMEV tools v4_9_0.45. Gene Ontology (GO) was performed with Ingenuity Pathway Analysis (IPA) software.

Results: Significant mRBP gene expression changes were detected in S vs NS, COPD vs NS and COPD vs S comparisons (n genes = 249, 464 and 445, respectively). Genes with FC ≥ |2.0| constituted 16% of those detected in S vs NS and more than 40% in COPD vs NS and COPD vs S (n = 40, 214 and 186, respectively). Interestingly, the majority of these genes were downregulated in COPD vs NS (n = 137, 64%) and COPD vs S (n = 150, 80%) while only 17% were downregulated in S vs NS (n = 7). Correlation analysis identified discrete clusters of co-expressed genes. GO analysis revealed significant enrichments in canonical pathways both specific and shared across the comparisons.

Conclusion: The novel characterization of mRBPs expression in airway epithelium and further definition of their functional impact is necessary to understand how PTR contributes to chronic inflammatory lung disease and whether it can be targeted therapeutically.

TP0712 | Dysregulation of NLRP3 inflammasome pathways in patients with severe asthma

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Background: Severe allergic asthma (SA) represents a chronic inflammatory lung disease characterized by recurring symptoms of reversible airflow obstruction, airway hyperresponsiveness and remodeling. Exuberant activation of inflammasome pathways, and specifically the NLRP3 component, is critically involved in inflammatory cytokine release, such as, IL-1β and IL-18, and in the development of airway inflammation in experimental asthma. Still, the role of NLRP3 and its signaling components in severe asthma remains elusive. In the present studies, we investigated the activation of NLRP3 in peripheral blood monocytes and in the airways of patients with SA, and the molecular mechanisms underlying its suppression.

Method: We obtained peripheral blood, bronchoalveolar lavage fluid (BALF), serum and bronchial biopsies from Severe Asthmatics (SA), Mild Moderate Asthmatics (MMA) and Healthy controls (HC) (n = 10 ± 3). The expression and activation of NLRP3 was investigated using immunofluorescent staining (IMF) and antibodies against NLRP3 and ASC to detect ASC speck formation, and analyzed by confocal microscopy. The release of IL-1β, IL-18, IL-10 and the IL-1β receptor antagonist (IL-1ra) were measured in the BALF and serum by ELISA. $CD14^+$ monocytes were isolated from the peripheral blood and activated with LPS (priming signal) and ATP (activating signal). NLRP3 activation and cytokine expression were examined by quantitative RT-PCR analysis, IMF staining and ELISA in monocyte culture supernatants.

Results: We observed significantly increased formation of ASC specks, indicative of NLRP3 activation, in lung sections from patients with SA, compared to HC. Moreover, IL-1β and IL-18 were significantly increased in the BALF and serum of SA and MMA patients. Notably, NLRP3 activation was upregulated in $CD14^+$ monocytes from SA patients at baseline, and further increased upon LPS and ATP activation. In contrast, the anti-inflammatory cytokine IL-10 was significantly decreased in monocyte cultures from SA patients upon NLRP3 activation, as compared to MMA and HC.

Conclusion: Our studies reveal, for the first time to acknowledge, aberrant activation of the NLRP3 inflammasome pathway in peripheral blood monocytes and the airways of SA patients, concomitant with decreased IL-10 responses. Dysregulated inflammasome activation in SA patients may serve as an essential target for therapeutic intervention.

TP0713 | The inflammatory effects in response to different exercise intensities: A systematic review

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Background: Exercise leads to a robust inflammatory response mainly characterized by the mobilization of leukocytes and an increase in circulating inflammatory mediators produced by immune cells and directly from the active muscle tissue. Both positive and negative effects on immune function and susceptibility to minor illnesses were observed. While engaging in moderate activity may enhance immune function above sedentary levels, excessive amounts

of prolonged and high-intensity exercise may impair immune function. The goal of this systematic review was to clarify the inflammatory effects in response to different exercise intensities.

Method: A systemic search examining exercise and inflammation was performed on PubMed and completed on July 31st, 2017. Eighteen articles were included, and their quality was assessed. The specific components that were examined included circulating blood levels of cytokines, leukocytes, creatine kinase (CK) and C-reactive protein (CRP).

Results: Most of the intervention studies showed changes in the assessed biomarkers, although these changes were not always consistent. White blood cells (WBC) had an increase immediately after intensive exercise (> 64% VO_2 max), without alteration after moderate exercise (46 - 64% VO_2 max). The results suggested an elevation of the pro-inflammatory cytokines, namely IL-6, followed by an elevation of IL-10 that were more evident after intensive exercise bouts. CRP increased both after intense and moderate exercise, with peak increases up to 28 h. CK increased only after intensive and long exercitation.

Conclusion: It is suggested a particularly caution due to increased susceptibility to illness when higher exercise intensities are used.

TP0714 | Allergen activated eosinophils promote expression of extracellular matrix proteins in airway smooth muscle cells and induce their migration in asthma

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Background: Airway structural changes or remodeling in asthma include subepithelial fibrosis, increased smooth muscle mass, enlargement of glands, neovascularization, and epithelial alterations. Airway eosinophilia is a prominent feature of allergic asthma. Eosinophils may directly, by adhesion, and indirectly, by mediators, act on airway remodeling. Airway smooth muscle (ASM) cells migration and expression of extracellular matrix (ECM) proteins may be influenced by airway eosinophilia.

Method: 8 allergic asthma patients (AA) and 8 healthy subjects (HS) were examined and underwent bronchial allergen challenge. Blood eosinophils were isolated using high-density centrifugation and magnetic separation. Individual combined cultures of eosinophils and healthy ASM cells as well as pulmonary fibroblasts were prepared. Migration was evaluated after 24 h using wound healing assay. For gene expression analysis ASM cells and eosinophils were lysed and total RNA purified after 24 h of incubation with eosinophils. Gene expression was evaluated using qPCR analysis.

Results: Gene expression of *TGF-β* was statistically significant increased in eosinophils isolated from allergic asthma patients after bronchial challenge compared to baseline and healthy subjects. Gene expression of ECM proteins (*COL1*, *COL3*, *COL5*, *FN*, *DCN*, *VCAN*, *α-SMA*) in ASM cells was significantly ($P < 0.05$) promoted after incubation with activated asthmatic eosinophils compared to baseline and healthy subjects. After the bronchial challenge, asthmatic eosinophils significantly induced migration of ASM cells (15.52 ± 3.43 vs 36.31 ± 3.47, $P < 0.05$) compared to healthy subjects.

Conclusion: Allergen activated eosinophils were more active than in baseline and those from healthy subjects. Activation of eosinophils could trigger the promotion of ECM proteins expression in ASM cells as well as ASM cells migration.

TP0715 | The effect of SERPINB1 protease inhibitor on the inflammatory response genes in bronchial epithelial cells

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Background: Allergen proteases are important factors in airway inflammation. After inhalation of allergen proteases, epithelial cells, which is the first line defense in the airway, synthesize protease inhibitors and protect the cells against the destructive effect of proteases. Using microarray and real-time PCR we have previously

TABLE 1. The effect of SERPINB1 gene on cytokine, chemokine, and growth factor expressions in BEAS-2B cell line (the gene expressions of each hour were evaluated among themselves) (<->: no change observed)

	12 H			24 H			36 H			48 H		
BEAS-2B	Derp1	siRNA	siRNA+Derp1	Derp1	siRNA	siRNA+Derp1	Derp1	siRNA	siRNA+Derp1	Derp1	siRNA	siRNA+Derp1
IL-6	3.1	10.35	14	1.8	1.67	2.11	1.7	18	5.7	1.1	5.2	2.3
IL-8	3.22	13.92	20.93	1.6	1.1	2.3	3.2	16.6	5.7	1	8.6	2.8
GM-CSF	1.24	3.14	9.13	3.1	4	4	0.3	10	2.5	1.4	2.8	3.6
RANTES	0.28	3.68	12.28	21.8	4.1	16.3	0.3	21	16	1.1	4.6	5.3
PDGF-ß	0.90	0.1	1.44	0.3	0.5	1.8	2.3	6.5	3.9	1.05	5	2.3
TSLP	1.17	0.44	0.35	2.1	0.9	2.4	1.12	2.9	5.9	1.3	1.3	2

TABLE 2. The effect of SERPINB1 gene on the protein levels of IL-6 and IL-8 in BEAS-2B cell line (the protein levels of each hour were evaluated among themselves)(<->: no change observed)

	12 H			24 H			36 H			48 H		
BEAS-2B	Derp1	siRNA	siRNA +Derp1	Derp1	siRNA	siRNA +Derp1	Derp1	siRNA	siRNA +Derp1	Derp1	siRNA	siRNA +Derp1
IL-6	1.05	3.5	3.03	1.06	1.04	1.06	0.9	0.48	0.42	1.16	0.6	0.44
IL-8	1.21	5.27	3.8	1.03	2	1.03	0.9	1.57	1.3	1.15	3.5	1.5

demonstrated that the stimulation of Der p1 (Dermatophagoides pteronyssinus 1) allergen changes the expression of a protease inhibitor, SERPINB1, in bronchial epithelial cells. In this study, we aim to determine the effect of SERPINB1 on the release of cytokines, chemokines and growth factors involved in the inflammatory response.

Method: Bronchial epithelial cells (BEAS-2B) were transfected by SERPINB1-siRNA when they reached 60-70% confluency. Transfection efficiency was shown by SERPINB1 expression. The effect of siRNA-transfection was determined using negative siRNA. Transfected and un-transfected cells were stimulated with Der p1 (5 μg/mL) for 12, 24, 36 and 48 hours. IL-6, IL-8, GM-CSF, RANTES, PDGF-ß, and TSLP gene expressions were measured by qPCR and IL-6 and IL-8 protein expressions were determined by ELISA.

Results: Results are shown in Table 1 and Table 2.

Conclusion: Cytokines, chemokines and growth factors which play a role in the inflammatory response have an indirect relation with the expression of SERPINB1 gene.

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TP0716 | A new approach for understanding the crosstalking signalling bone morphogenetic proteins pathways between different forms of specific and non-specific challenge test

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Background: Asthma is a chronic disease, in which various cytokines, including Transforming Growth Factor β(TGF-β), are responsible for inflammation.

Bone Morphogenetic Proteins(BMPs) are members of the TGF-β superfamily.

In the canonical pathway both TGF-βs and BMPs transduce signal similarly through the SMAD superfamily and common co-mediating protein SMAD4.

SMAD2 and 3 are recognized by the TGF-β receptor type 1(TGF-βR1) and type 2(TGF-βR2).

The signal from BMPR receptors is conducted through complexes with SMAD1,5,8.

Our primary objective was to assess the correlation between the serum level of BMP4 and BMP7 and the selected SMAD(SMAD2,4 and 5) in different time points.

Secondly, we wanted to assess whether another SMAD proteins could also take part in the BMPs signalling process.

Method: There were recruited 60 patients with asthma and 48 healthy volunteers.

Spirometry, skin prick tests, allergen and methacholine challenge tests were performed in compliance with EAACI, ERS and ATS guidelines.

Personalized clinic surveys including ACT™ were performed.

Blood samples were collected to EDTA-KE filled test tubes before and 1 h/24 h/48 h after the allergen/methacholine challenge test.

Evaluation of BMP4 and BMP7 serum protein levels was performed using specific ELISA immunoassay kits.

RNA isolation was performed with the standard extraction protocol.

Real Time qRT-PCR was performed using Phusion High Fidelity DNA Polymerase and EvaGreen® dye with specific primers. We used the 2-ΔΔCT method for statistical analysis of the qRT-PCR results

Results: There were statistically significant differences in BMP7 levels (P = 0.038106) and in BMP4 expression (P = 0.042026) between healthy controls and asthmatics before the challenge.

Unexpectedly, we found two statistically significant correlations: between the BMP4 serum level and SMAD2 (R = 0.35; P = 0.0004) and between the BMP7 serum level and SMAD2 (R = 0.24; P = 0.034) before the challenge in all the subjects(healthy and asthmatics).

We didn't find any correlation between the BMP4 and BMP7 serum levels and SMAD proteins after the methacholine and allergen challenge tests

Conclusion: There were differences in BMP7 serum level and the BMP4 expression between asthmatic and healthy group, which could indicate the role of BMPs in the etiopathogenesis of asthma.

The correlation between both BMP4 and BMP7 and SMAD2 protein, which is a part of TGFßR-SMAD2/3 pathway, suggested that BMPs could also stimulate formatting complexes with another SMAD superfamily proteins, not only with SMAD1,5,8.

TP0717 | Comparison of the oxidative stress response induced by tert-butyl hydroperoxide in airway resident and inflammatory cells

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Background: Oxidative stress plays an important role in many inflammatory diseases including asthma where Reactive Oxygen Species (ROS) are formed by all airway resident and inflammatory cells. We aimed to compare oxidative stress potential of airway epithelium, fibroblasts, monocytes and eosinophils.

Method: Cell lines of Epithelial cells, monocytes and eosinophils were maintained in RPMI 1640 medium; fibroblasts in EMEM. Each cell line was treated with various doses of a known ROS inducer from 0 mM to 5 mM of tert-butyl hydroperoxide (tBHP) for 1 and 2 hours. Fluorescence measurement of the ROS was done by 2′,7′-Dichlorodi hydrofluorescein diacetate (DCFHDA). Viability and cytotoxity were determined by tBHP, MTT, LDH assays and Etbr/Calcein staining.

Results: Each cell line treated with tBHP showed a significant increase in ROS generation compared to untreated controls. We found that tBHP was able to induce ROS accumulation with a time-dependent manner. Even the lowest concentration (0.0125 mM) of tBHP significantly induced ROS levels, especially in inflammatory cells. However, viability of cells decreased after 0.05 mM concentration of tBHP. Resident cells were able to resist higher concentrations without losing viability.

Conclusion: Each cell line showed a different response to oxidative stress inducer showing different thresholds for cell death and ROS production. Resident cells are more resistant to oxidant stress compared to inflammatory cells. Oxidative stress varies according to the cell type, dose of tBHP and duration of exposure. Understanding these differences are essential for determining the contribution of different lung cells in oxidative damage and antioxidant response to the oxidative stress.

TP0718 | The role of γδ T cells in immunopathogenesis of respiratory allergies

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Background: Allergy is often called as disease of our century. In 2014 in Georgia registered 10 589 cases of asthma and asthmatic status, between them was recorded 3137 new accidents.

The major aim of our research represented to investigate the role of γδ T cell subset in the pathogenesis of respiratory allergies. γδ T cells have recently became the focus of attention in the immunopathogenesis of respiratory allergies. Recent studies have shown that T cells can comprise up to 50% of the T cells within epithelium or mucosa-rich tissues and less than 10% in peripheral blood. Such amount of γδ T cells in tissues mentioned above clearly suggesting their important role in forming and functioning epithelial and mucosal immunity. Considering this all, there is a consensus that the γδ T cells have a significant function in the immunopathogenesis of respiratory allergies.

Along with other mediators, the γδ T cells are an important source of IL-17, which role is very important, because IL-17 expression is increased in the lung, sputum, bronchoalveolar lavage fluid and sera in patients with asthma. The severity of disease is positively correlated with IL-17 expression levels.

Method: In the Peripheral blood mononuclear cells from 30 patients with bronchial asthma and 20 age-matched healthy volunteers were determined the subsets of γδ T cells with activation marker CD69 and formation of IL-17 in γδ T cells analyzed by FACScan flow cytometer (B&D).

Results: According our results in the peripheral blood of patients with suffering disease, there is no significant increase or decrease in the total number of T lymphocytes, but its subtypes - γδ T cells are increased compared to the control group. It is noticeable the ratio changing between the subpopulations inside it. Compared to the control group, the number of Vδ1 and Vδ2 T cells is increased. Vδ1 T cells activation level is reduced compared to the control group and increased Vδ2 T cells activation level. Both subgroups of γδ T cells are responsible for the production of IL-17 and the same way have been found to increase IL-17 production by Vδ1 T cells in the patients with bronchial asthma.

Conclusion: Our data indicate that the γδ T cells involved in the immunopathogenesis of bronchial asthma.

TP0719 | House dust mite-derived HODEs shape the development and progression of allergic airway inflammation

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Background: House dust mite (HDM) is the major indoor-allergen source inducing allergic asthma. Chemically, aside from (glyco) proteins, HDM consist of a large variety of lipids. Lipids can initiate and modulate allergic reactions alone or as adjuvants for single allergens. In addition, several HDM allergens bear hydrophobic domains, allowing them to interact with lipids. 9- and 13-Hydroxyoctadecadienoic acid (9-HODE and 13-HODE) are enzymatic metabolites of linoleic acid (LA, 18:2n-6). HODEs are endogenous lipid mediators released by several lung cell types.

Atopic asthmatics have increased serum levels of 13-HODE. In experimental models, 13-S-HODE induced pulmonary hyperresponsiveness and severe asthma. Here, we report for the first time the isolation of 9-/13-HODE from HDM and show how HDM-HODEs modulate allergic inflammation alone and in combination with the major HDM-allergen Der p 2.

Method: To examine the role of HDM-derived lipids in allergic inflammation, we performed a chloroform/methanol/water extraction from *Dermatophagoides pteronyssinus* bodies, the organic phase was fractionated on silica gel and HPLC, and chemically characterized by gas chromatography and fmass spectrometry. The biological activity of the lipids was analyzed using *in vitro* screening systems based on murine bone marrow-derived mast and dendritic cells. Additionally, HDM-derived lipids were tested for allergen-adjuvanticity in the human bronchial epithelial cell line Calu-3 and in primary normal human bronchial epithelial cells (NHBEs).

Results: Fractions containing 9-/13-HODE significantly increased IgE-mediated degranulation of murine mast cells. In the Calu-3 cell line, HODEs induced IL-6 and CXCL8 release and morphological changes that were enhanced by co-administration of natural Der p2. In NHBEs (n = 1) cultured in the presence/absence of IL-13, 9-/13-HODEs alone and in combination with Der p2 affected the cell monolayer integrity, the gene-expression of Occludin, Claudin-4 and the goblet cell marker CLCA1. In IL-13-treated NHBEs, HODEs induced an increased release of Eotaxin. In non-IL-13-treated cells, HODEs provoked a reduction of baseline levels of GM-CSF, IL-1b, IL-6, CXCL8, MCP-1 and TNF-a. This effect was reversed by treatment with Der p 2.

Conclusion: Our study is the first to show HDM as an exogenous source of bioactive HODEs and evidences how HODEs alone and in combination with allergen could shape the development and progression of allergic asthma.

TP0720 | The feature of the immune status of the phenotype of bronchial asthma with obesity

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Background: Obesity is an important factor determining the phenotype of the severe asthma, worsens her control, is a cause of a violation of the physiology of respiration, exacerbating the pulmonary obstruction. Objective: to study the immune status in patients with bronchial asthma (BA) with obesity.

Method: we examined 86 patients with BA of different severity. The obesity was diagnosed with the use of Quetelet index, and the coefficient of fat deposition centralization. The first group included the patients with the normal weight of the body (n = 30), the second group consisted of patients who are overweight (n = 30), the third group was made of patients with the obesity of I—II degree (n = 26). 22 healthy volunteers formed the control group. We used the complex of clinical, allergological and immunological examination methods.

Results: In the group of BA obese patients there was found a significant increase of lymphocytes level by 21.8% (36.4 ± 2.5%), of CD3 + by 19.9% (83.8 ± 2.0%), of CD19 + by 37.5% (16.5 ± 2.1); increased levels of serum IgA, g/l (2.14 ± 0.35) and decrease in total IgE IU/mL (96.80 ± 11.47) in comparison with BA patients with the normal body weight (28.6 ± 2.4% 67.2 ± 3.2%; 10.3 ± 1.3% — respectively) ($P < 0.05$); (IgA g/l 1.88 ± 0.12; IgE IU/mL 211.79 ± 197.63). Analyzing phagocytic activity of neutrophils, significant growth of metabolic activity of neutrophils and the index of neutrophils activation was found out in all the groups of BA patients in comparison with healthy patients. At the same time the reserve of oxygen-dependent metabolism of neutrophils in BA overweight patients and obese patients was low. The correlation analysis showed the direct dependence of CD3 + ($r = 0.59$; $P < 0.01$) and CD4 + ($r = 0.49$; $P < 0.01$) levels on the waist size and thighs size and the coefficient of fat deposition centralization. The strong correlation was found out between CD19 + and the coefficient of fat deposition centralization ($r = 0.9$; $P < 0.01$)

Conclusion: These investigations showed that the combination of BA and obesity is followed by the increase of the system inflammation, which is proved by the increased number of leucocytes, their T and B-cellular links, the parameters of oxidative metabolism of neutrophils and the decrease of the reserve possibilities of phagocytosis.

TP0721 | Metabolic activity deviations in patients with hormone-dependent asthma

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Background: Bronchial asthma (BA) is one of the most important medical and social problems. Severe forms of BA requires massive therapy with glucocorticosteroids (GCS), which can lead to immunosuppression followed by associated diseases. Also with continuous use of GCS in high doses, the metabolic functions of cytochrome P450, the main enzyme of biotransformation, may change, which may affect the effectiveness of the drug therapy used. CYP3A4 activity can be determined by the ratio of the concentration of metabolite and substrate CYP3A4 in the blood. Endogenous cortisol was selected as a substrate, and its metabolite was 6β-hydroxycortisol. The greater the metabolic ratio, the higher the activity of the enzyme under study. The aim of the work is to study the body's metabolic system in patients with hormone-dependent BA.

Method: The study group included 34 patients of both sexes, the average age of 45 years, with hormone-dependent BA. The control group included 34 healthy volunteers of both sexes, with an average age of 35 years. For phenotyping, a method developed by the authors for the quantitative determination of cortisol and its plasma metabolite in blood plasma was used by HPLC-MS/MS.

TABLE 1.

	Cortisol plasma level, ng/mL		Metabolic ratio (6β-hydroxycortisol/cortisol plasma level)	
Value	Study group	Control group	Study group	Control group
Mean	103.38	69.62	5.71*	3.83*
G. mean	95.95	66.28	4.96	3.41
SD	45.34	21.85	3.55	1.75
CV, %	43.86	31.38	62.26	45.61
Median	88.12	66.32	5.38	3.92

* Statistically significant differences based on T-test (α = 0.95)

Results: As a result of the study, data on CYP3A4 activity were obtained, which are listed in the table. As can be seen from the data, metabolic activity in patients with hormone-dependent BA is increased relative to the control group. The T-test result (α = 0.95) indicates the presence of statistically significant differences between the mean values of the metabolic relations in patients and the control group: F = 2.768, *P* = 0.007. This circumstance may lead to the ineffectiveness of pharmacotherapy with various CYP3A4 substrates.
Conclusion: In patients with hormone-dependent BA, receiving therapy with systemic corticosteroids, an increase in CYP3A4 activity was found compared with healthy volunteers. The ratio of the level of endogenous 6β-hydroxycortisol to cortisol in the blood plasma of patients with asthma is 67% higher than in healthy volunteers. Thus, the determination of CYP3A4 activity should be carried out in patients with hormone-dependent BA in order to correct the dose of prescribed drugs both in therapy with GCS drugs and in polyphragmas, since an increase in the metabolic activity of CYP3A4, which participates in biotransformation of about 70% of known drugs, will lead to changes in the concentration of prescribed drugs in plasma.

TP0723 | Investigation on the immunological effects of regular physical exercise

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Background: Growing evidence shed light on the significant effects of physical activity on immunomodulation. Consequences may largely depend on the type of activity, its intensity and duration. However, little information is available regarding the immunological effects of sporting activities in older ages. The aim of our study was to examine the changes in a wide spectrum of lymphocyte subtypes after a period of regular workout among healthy women of different ages.
Method: In a cross-sectional study, we enrolled 34 young adult women (between ages of 19-23 years), 8 of them were a player of a team in Hungarian Women's Volleyball League, while 26 of them were not engaged in regular physical activity. Additionally, we enrolled 16 elderly women (between ages of 60-75 years) not engaged in regular physical activity. During a follow-up study, 17 from the group of non-athlete young adults completed a 12-week Pilates workout program, while the group of elderly women took part in a 6-week lightweight conditioning gymnastic exercise program once a week. The percentages of peripheral natural killer (NK), NKT cells, T and B lymphocyte subtypes (early-/late-activated T, naive and memory T, cytotoxic T (Tc), T-helper (Th)1, Th2, Th17, T regulatory type 1 (Tr1), CD4 + CD127-CD25^{bright} Treg, as well as naive and memory B cells) were determined by flow cytometry based on the staining of extracellular markers and intracellular cytokines.
Results: The investigated baseline parameters did not show significant differences between athlete and non-athlete young adults. In the elderly, levels of CD3 + 6B11 + NKT cells were lower, while ratios of CD4 + Th/CD8 + Tc cells were higher compared to the values of younger individuals. At the end of exercise programs, changes observed among 60-75 year-olds were more pronounced compared to alterations developed in younger subjects. In elderly women, percentages of IgD+ naive B cells decreased, while levels of CD27 + switched-memory B cells increased. Furthermore, proportions of CD4 + IL-4 + Th2 cells increased, while levels of CD8 + IFN-gamma+ Tc cells and immunosuppressive CD4 + CD127-CD25^{bright} Treg cells decreased as the result of regular exercise.
Conclusion: Differences observed after lightweight exercise programs reflect a presumably enhanced immunoreactivity and increased ability for immune responses, especially in older ages. The research was supported by the GINOP-2.3.2-15-2016-00062 project. The project is co-financed by the European Union from the European Regional Development Fund.

SUNDAY, 2 JUNE 2019
TPS 07
LIVING WITH SKIN DISEASE

TP0725 | Hereditary angioedema awareness in turkish emergency department physicians and the Results of a brief video assisted education

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Background: Hereditary angioedema (HAE) is a rare life-threatening disease. Laryngeal edema can lead to asphyxiation and death. Therefore, appropriate diagnosis and prompt management should be performed. Accordingly, emergency physicians should be able to distinguish different types of angioedema and effectively treat rare presentations like HAE. We aimed to assess the HAE awareness among Turkish emergency department physicians and the effects of a brief video assisted education on this awareness.

Method: We contacted emergency physicians in two different ways in order to conduct a Pre-test: A face to face interview was provided with the majority (350) of them during their 2018 National Congress. The others were invited by e-mail to participate a web survey. The prior survey (Pre-test) included 12 multiple choice questions regarding angioedema and HAE. After they had watched a short video about HAE and its treatment, they answered the same questions once more in the context of a Post-test with a face to face interview.

Results: 505 physicians participated the pre-test survey however 350 were able to take post-test after watching the educational video. Most of the physicians (80%) knew that the most common type of angioedema was histaminergic and standard treatment included antihistamines and corticosteroids.

In pre-test, two out of five (40.8%) of participants answered that they would consider HAE in case of an angioedema which doesn't respond to antihistamines and corticosteroids; this rate increased to 94% in post-test.

In pre-test, a very few (4%) of the participants were aware of the HAE diagnostic criteria and only half of them (48%) has gained a sufficient knowledge about it after the video film. The questions about acute attacks of HAE and prophylactic treatments were correctly answered by 30% and 11.5% of the physicians respectively in pre-test; the correct response rate increased to 84.6% and 83.6% respectively in post-test.

Conclusion: This survey revealed that the awareness about HAE diagnosis and treatment is not sufficient among emergency physicians. Considering the possible fatality of the attacks, a training program about this rare disease is of major importance for emergency departments.

TP0726 | Persistent lips angioedema of 1.5 years of evolution

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Case report: We visited a 35-year-old woman with persistent swelling lips and perioral erythema of 1.5 years of evolution; described as persistent angioedema. There wasn't dyspnea or other systemic symptoms. She didn't respond to several cycles of oral corticoids or antihistaminic. She wasn't carrier of any implant or has any aesthetic intervention. A week before she went to the dentist for dental extraction. In the physical exploration there was inflammation and swelling lips with erythema, there was no eyes or uvula angioedema.

Prick test were performed (only positive for 8 × 6 mm mites, 7 × 6 mm grass, His 4 × 4 mm, negative control) and food prick test was negative.

Blood tests were performed with normal results: Hemogram, hemostasis, biochemistry (liver and renal and function), thyroid antibodies and hormones, ANAs, FR, complement and its fractions. Other results IgE 23.6 KU/L, triptase 11.7 n/L. Specific IgEs were negative for anisakis, wheat, latex and Ascaris. PCR was 8.8 mg/L (high).

Serologies: B and C hepatitis HIV, Syphilis: negative.

Stool test: no helminths, saprophytic flora.

We asked for a lip biopsy: scaly epithelium without injury. Lymphocytotic accumulation of granulomatous aspect to stroma, absence of necrosis and absence of pathogenic microorganisms.

CT chest, endoscopy and colonoscopy were normal.

This is a "Granulomatous Cheilitis" or "Miescher Syndrome", is rare entity, of unknown cause and pathogenesis. Its variant is the Melkersson Rosenthal's Syndrome.

It appears on the 2nd and 3rd decades of life, especially on the upper lip. The diagnosis is by pathological anatomy; It has no specific treatment and it is important to make the differential diagnosis with tuberculosis, sarcoidosis and inflammatory bowel disease.

Now our patient is treatment with our Dermatology Department.

TP0728 | Hereditary angioedema in a real clinical practice

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Background: Hereditary angioedema (HAE) is a rare disorder with recurrent attacks of severe swelling commonly affecting the extremities, face, intestinal tract, and airways. Little is known about patients with HAE in Russia. The aim of this study was to assess clinical characteristics of patients with HAE in real clinical practice.
Method: We examined 18 adult outpatients (55% males) aged 18-59 yrs (mean age 37 yrs) referred to our secondary care center by general practitioners. C1-esterase inhibitor quantity and activity in blood were evaluated by immunoenzyme analysis.
Results: All 18 patients had HAE type 1 with mean C1-inhibitor concentration and functional activity 31% and 30% of normal respectively. Eighty nine percent of patients had a positive family history. First symptoms of HAE appeared at age 1-26 yrs (mean age 11 yrs, 50% before 10 yrs, 78% before 20 yrs). HAE was diagnosed in 1-54 yrs (mean 23 yrs) after onset of the disease. Triggers of swelling were trauma - 78% and physical activity - 67%, stress — 22%, injections and insect stings — 11%, flu - 6%, dental manipulations - 6%, overnutrition — 6%. Frequency of HAE attacks varied 1-20 each year per patient (mean 7 per year/patient). Locations of swelling were extremities — 63%, face -50%, intestinal tract — 72%, larynx - 67%. One patient underwent tracheotomy for 6 times, other patient — for 2 times. One of the patients has 2 laparotomies due to HAE attacks during lifetime. Maintenance therapy in most patients included tranexamic acid, 2 patients were treated by danazol for many years. Icatibant was used in 14 patients and C1-concentrate — in 1 patient with acute attacks of HAE.
Conclusion: HAE may be a debilitated disorder. There is a significant delay (more than 20 yrs) between the onset and diagnosis of HAE. Most common therapy was tranexamic acid for maintenance and icatibant for acute attacks of swelling.

TP0729 | Real world data of Canadians living with hereditary Angioedema: Part 4- Treatment satisfaction

Brosz K[1]; Baidou J[1]; Howlett L[1]; Rowe A[1]; Steele K[1]; Falbo J[2]; Santucci S[2]; Valois J[2]; Yang WH[2,3]

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Background: Hereditary angioedema (HAE) is a chronic spontaneous life-threatening disease. Due to the unpredictable nature associated with the disease it can have a significant impact on a patient's quality of life. We sought to better understand the overall satisfaction of treatments from a patient's perspective.
Method: In 2017-2018, data were collected through voluntary online surveys of children, youth, and adults who live with HAE and their caregivers in Canada. The following data were based solely on adult participants.
Results: Once a proper diagnosis was obtained following patient navigation and treatments were established the annual number of days missed from work or school decreased by an average of 48%, the amount of phone calls to doctor's offices decreased 60%, the occurrence of unscheduled visits to health care professionals decreased 75%, the frequency of emergency room visits decreased 50%, and the number of hospitalizations decreased 67%. Most patients reported they were satisfied with the frequency they must use their HAE treatments (31%) and satisfied with the effectiveness of their current treatments to prevent attacks (40%). Overall patients were satisfied (39%) and very satisfied (24%) with their current HAE treatment.
Conclusion: Results show patients are generally satisfied with the treatments they are currently receiving; however, there are still necessary improvements that can enhance a patient's quality of life. All results are limited to the respondents and may not represent the broader Canadian HAE population.

TP0730 | Real world data of Canadian's living with hereditary angioedema: Part 1- demographics

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Background: Hereditary angioedema (HAE) is an unpredictable and serious genetic disorder affecting approximately 1:10 000 to 1:50 000. It is an autosomal dominant disorder due to C1 inhibitor deficiency. Clinically, it is manifested by painful, unpredictable edema of the face, larynx, abdomen, genitals and extremities. It can be debilitating and if left untreated, may be fatal. We sought to better understand the demographic profiles of patients living with HAE in Canada.
Method: In 2017-2018, the first National Canadian HAE survey was electronically sent to all HAE Canada members. Data from respondents was collected and analyzed using percentage of total surveys.
Results: The demographic location of HAE patients living in Canada includes Ontario, Alberta, Manitoba, British Columbia, Nova Scotia, Quebec, Saskatchewan and Newfoundland and Labrador. 140 respondents indicated their relationship to HAE as; 81% are adults living with HAE, 10% are caregivers of an adult living with HAE who lives with them, 2% are caregivers of an adult living with HAE who does not live with them, 2% are adults awaiting a diagnosis, and 4% are other or unknown. Among, 109 respondents 79% indicated they are female and 21% are male. When asked about their HAE type, 60% were found to have type 1/2 C1-inhibitor protein deficiency, 26% have HAE with normal C1-inhibitor, 10% unsure, and 4% have acquired angioedema.

Conclusion: This survey helps to better understand the current demographic profile of patients living with HAE. However, data interpretation is limited due to uncertainty of necessary sample size required to be representative of the true population. Overall, our results demonstrate that HAE patients can be found across Canada and that the majority of patients in this survey are aware of their diagnosis.

TP0731 | Real world data of Canadian's living with hereditary angioedema: Part 2- attack profile

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Background: Hereditary Angioedema (HAE) is a rare genetic disorder that is characterized by episodes of unpredictable painful swelling in different body parts. To better understand the challenges of Canadians living with HAE our objective was to gather real world data that will provide insight into the attack profiles of a HAE patient.
Method: In 2017-2018, the first National Canadian HAE survey was electronically sent to all HAE Canada members. The following data were based solely on adult participants.
Results: Among 104 participants with HAE they reported a diagnosis of: Type 1 or 2 C1-inhibitor protein deficiency (60%), HAE with normal C1-inhibitor (26%), acquired angioedema (4%), and unsure of diagnosis (10%). In the last year, 78% were symptomatic, 11% were asymptomatic, and 11% were unsure. Regarding the frequency of attacks: 61% had 7 or more attacks, 22% had 1-6 attacks, 6% had no attacks, and 10% were unsure. Identifiable attack triggers vary from stress (87%), typing/writing (78%), trauma (70%), illness (61%), medical procedures (61%), anxiety (55%), and Ace Inhibitors (6%). Other factors that increase HAE symptoms include menopause (9%), estrogen contraceptives (33%), and menstruation (47%). To treat these attacks, 84% use an agent, compared to 16% who do not.
Conclusion: Our findings demonstrate the majority of participants are knowledgeable in identifying their triggers and managing their attacks. Results show improvements are necessary for proper diagnosis and awareness of the disease. Since the number of individuals living with HAE is estimated, our data are limited to the respondents and may not represent the broader Canadian HAE population.

TP0732 | Co-existence of type 3 hereditary angioedema and polycystic ovary syndrome

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Case report: An adolescent patient with the signs of oligomenorrhea with irregular menstruations, obesity, hirsutism and acanthosis nigricans was diagnosed with polycystic ovary syndrome (PCOS) and prescribed ethinyl estradiol & cyproterone acetate containing oral contraceptive (OC). At 16th day of treatment, the patient developed angioedema starting from the left periorbital area spreading to the face, neck and chest and leading to dyspnea. Adrenaline, antihistamine and corticosteroid treatments were ineffective. In the family history, the patient's mother and 2 cousins also had angioedema attacks. C1 esterase inhibitor concentrate was administered with a diagnosis of hereditary angioedema. C4 level, C1 esterase inhibitor level and activity were normal. In genetic analysis, a heterozygote Thr328Lys mutation on Exon 9 was identified and a diagnosis of type 3 HA was considered. Then the patient treated with metformin for obesity and OC with only progesterone for PCOS. She has had no additional angioedema attacks in the follow-up period up till now.
Conclusion: Oral contraceptives with estrogen may induce the life-threatening first attack of HA type 3. Personal or family history of angioedema should be checked before prescribing OCs. HA patients should also be informed about factors triggering angioedema.

TP0733 | Impact of the body mass index in patients with mastocytosis

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Background: The BMI is an attempt to quantify the amount of tissue mass (muscle, fat, and bone) in an individual, and then categorize that

person as underweight, normal weight, overweight, or obese based on that value. There were 2 aims of the study: 1. analysis of the relationship between BMI and distinct clinical forms of mastocytosis, 2. the relationship between malnutrition and weight loss in clinical forms of mastocytosis in clinical forms of mastocytosis analyzed in the registry of ECNM.

Method: A total of 2985 patient with mastocytosis were enrolled. 1282 subjects had calculated BMI data, 2807 malabsorption data and 2807 weight loss >= 10% within last 12 months data were included. The correlations of BMI ≤ 18.5 with Hb and alkaline phosphatase were assessed.

Results: Malnutrition was recognized only in 3.2% in the study group. In group with malabsorption 67% patients have weight loss >= 10% within 12 months. Only 3.4% of the patients had BMI < 18.5. There were positive correlation between BMI < 18.5 and hemoglobin and alkaline phosphatase.

Conclusion: Patients with mastocytosis should be asked for the weight loss ≥ 10% within last 12 months and looked for malnutrition.

TP0734 | Psychoactive drugs use in patients with chronic urticaria or suspected drug hypersensitivity

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Background: Evaluate the use of psychoactive drugs in patients with Chronic Urticaria (CU) or Suspected Drug Hypersensitivity (DH) followed in the Immunoallergology department.

Method: Retrospective study of a sample of patients followed for CU or DH. Comparison with Control group (patients followed for asthma/rhinitis). Data from the clinical history and consumption of psychoactive drugs were evaluated through electronic records and prescription. The $\chi 2$ test with 95% confidence interval was used to compare variables.

Results: CU: 70 patients; 50 (71%) women; average age 44 years (18-85 years). 26 (37%) used some type of psychoactive drug regularly and 19 (27%) more than one group of drugs; 21 (30%) used antidepressants, 24 (34%) anxiolytics and 6 (8%) hypnotics.

DH: 70 patients; 51 (73%) women; average age 45 years (19-78 years). 29 (41%) used some type of psychoactive drug regularly and 6 (8%) more than one group of drugs; 13 (18%) used antidepressants, 20 (28%) anxiolytics and 15 (21%) hypnotics. Concerning suspected drugs 57 (81%) were suspected of hypersensitivity to only one drug whereas 13 (18%) had complaints with more than one drug class. In order of frequency antibiotics were implicated in 38 (54%) patients, followed by NSAIDs in 29 (41%) patients. Only 2 (3%) patients had complaints related to psychotropic drugs.

Control: 160 patients; 107 (67%) women; average age 40 years (19-84 years). 38 (24%) used some type of psychoactive drug regularly and 23 (14%) more than one group of drugs; 31 (19%) used antidepressants, 29 (18%) anxiolytics and 3 (2%) hypnotics.

Comparing the CU group with the Controls there was a significant difference in those who consumed some type of psychoactive drug (p 0.037) and in those who used more than one group of drugs (p 0.021); in the DH group there was only a significant difference (p 0.006) in relation to the consumption of some type of psychoactive drug regularly.

Comparing to Controls there was a significant difference in the consumption of anxiolytics (p 0.007) and hypnotics (p 0.016) in the CU group; and significant difference in hypnotics consumption ($P < 0.0001$) in the DH group.

Conclusion: The consumption of psychotropic drugs in Controls reflects the findings described in the general population in Portugal (22.9% of Portuguese suffer from psychiatric disorders). However, we observed that this consumption is significantly higher among patients with CU and DH; therefore, the psychological evaluation in the diagnostic and therapeutic approach of these patients may be important.

TP0735 | Facial edema and urticaria due to potassium-sparing diuretic

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Case report: Potassium-sparing diuretics are diuretic drugs that not promote the secretion of potassium into the urine. Spironolactone is a competitive antagonist of the aldosterone receptor and belongs to this class of diuretics. In addition to this, spironolactone is a synthetic, steroidal antimineralocorticoid agent with additional antiandrogen and weak progestogen properties, as well as some indirect estrogen and glucocorticoid effects, which is used primarily as a diuretic and antihypertensive, but also for the purpose of reducing elevated androgen activity.

Spironolactone is used worldwide and is known for its safety and good tolerability. There have been rare reports that spironolactone may induce hypersensitivity reactions

We report the case of a 71-year-old man who presented with several episodes of pruritus, erythema and facial edema following ingestion of spironolactone.

Because of cirrhotic process the patient received a four years spironolactone (100 mg/24 hours) treatment.

The skin symptoms usually developed within 1 to 2 hours of drug intake. Informed consent was obtained from the patient for skin tests and challenges.

Skin prick-tests with spironolactone (4 mg/mL) and intradermoreaction with this drug (0.4 mg/mL) were realized.

Simple-blind controlled oral challenge was realized with increasing doses of spironolactone.

All cutaneous tests were negative. Because of the negativity of the cutaneous tests, we decided to perform a controlled oral challenge

with 12.5 mg of spironolactone. After 30 minutes, the patient developed a general massive urticaria and anxiety. He was successfully treated with parenteral antihistamines.

We report one a case of immediate urticaria due to spironolactone.

We did not demonstrate IgE by skin testing, although the clinical symptoms were compatible with an immediate hypersensitivity reaction.

Despite the negative skin tests, hypersensitivity to spironolactone was demonstrated by an oral challenge with 12.5 mg.

TP0737 | Allergy to cloxacillin versus skin disease. A case report

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Case report: Background: Cloxacillin is a semisynthetic penicillin widely used. Hypersensitivity reactions to cloxacillin have been reported and the skin reactions are common. Erythema annulare centrifugum (EAC) is a rare cutaneous disease characterized by an eruption of variable duration. The eruption may be associated with taking medication or an underlying diseases (infections, autoimmune diseases, hormonal changes and malignant tumor) and its accompanying characteristic symptoms. The aim is compare the initial diagnosis relating to allergy with the final diagnosis performed in the Allergy Department, and the importance of the study of drug allergy. Method: A 39-year-old woman, personal history of beta-lactams allergy. Forty-eight hours after taking cloxacillin for pilonidal abscess, she started with fever, rhinorrhoea, odynophagia, headache and eruption on the back of the hands. After 4 days, all symptoms disappeared except for skin lesions that began to be discretely pruritic in the periphery. The eruption didn't improve with topical clotrimazole. She didn't associate it with other triggers. The physical examination showed on the back of both hands, well-defined annular plaques with elevated erythematous and scaly edges with clarification in the central area.

Results: Prick-test with standard typical pneumoallergens of our area and food groups: negative. Blood test with hemogram, basic biochemistry, thyroid hormones, rheumatoid factor, serum proteinogram, ANA and thyroid autoantibodies, complement study, tumor markers and immunoglobulins (IgA, total IgE, IgG and IgM): normal. Serologies: Positive to Epstein-Barr virus (VCA) IgG and IgM; and negative to Hepatitis B, C and Mycoplasma pneumoniae. Specific IgE (InmunoCAP®-ISAC) to Amoxicillin, Ampicillin, Penicillin G and Penicillin V; Skin prick tests and intradermal tests with PPL, MDM, penicillin, amoxicillin and cloxacillin: negative. Single-blind oral challenge test with cloxacillin: negative Biopsy: skin with parakeratosis, queratosis and irregular elongation of epidermal ridges. Superficial dermis, increase of capillaries with a minimum perivascular chronic inflammatory infiltrate.

Conclusion: We present a case of EAC confirmed by biopsy, probably secondary to acute infection by Epstein-Barr virus. It is interesting because is a rare entity. Allergy to beta-lactams was ruled out. We want to highlight the importance of doing allergy drug studies, to avoid unnecessary exclusion measures.

TP0738 | Psychosomatic aspects of allergic diseases in adult population of Kazakhstan

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Background: The aim of our study was to determine the psychosomatic characteristics of patients, suffering from different types of allergic diseases, using adapted version of Four-Dimensional Symptom Questionnaire (4DSQ).

Method: 84 adult patients with different allergic diseases were enrolled in our clinical-based study at allergological center "Umit", Astana, Kazakhstan in January 2018 — January 2019. Physical examination was conducted and detailed case records were completed in all patients. Adapted and translated version of self-administered Four-Dimensional Symptom Questionnaire (4DSQ) was used for psychosomatic health symptoms assessment. All patients signed written informed consent for publication.

Results: Basic demographic data showed that patients' mean age was 33.6 ± 13.6 years, with female predomination - 68 (80.9%) versus 16 (19.1%) male. The highest number of patients were diagnosed atopic dermatitis 32 (38.0%), followed by acute urticaria in 24 (28.5%) patients and perennial allergic rhinitis in 24 (28.5%) as well. Respiratory allergy, including bronchial asthma, was found in 20 (23.8%) patients and food allergy in 8 (9.5%). Average psychosomatic symptoms score was 62.9 ± 28.0 with minimum of 20 and maximum of 147 balls. Feeling down or depressed "sometimes" - noted 40 (47.6%) respondents, among them 16 (19%) had respiratory allergy symptoms and the same number with atopic dermatitis, 12 (14.2%) urticaria and 8 (9.5%) allergic rhinitis. For the same depression assessment question, 12 (14.3%) patients responded "often", and all of them had only skin disorders without any respiratory symptoms. The number of diagnoses does not fit to the number of answers due to one patient could have several diagnoses. Difficulties in getting to sleep experienced 40 (47.6%) patients, including 20 (23.8%) "sometimes", 8 (9.5%) — "regularly" and 12 (14.3%) — "often" answers.

Conclusion: Psychosomatic symptoms play an important role in the clinical manifestations of allergic diseases, especially depression symptoms are more evident in patients with skin allergy, compared to those with respiratory problems. Strategies to promote a multidisciplinary approach for health, especially improving general quality of life, sleep quality and depression are of great importance.

TP0739 | Blood marker for differentiating among eosinophilic granulomatosis with polyangiitis, hypereosinophilic syndrome, and toxocariasis

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Background: Eosinophil-associated diseases often involve systemic organs, such as skin, lung, liver, kidney, nervous system, etc. Under such a situation, it may be difficult to differentiate between the eosinophilic diseases. Multiple organ involvements are found in eosinophilic granulomatosis with polyangiitis (EGPA) and hypereosinophilic syndrome (HES). Visceral larva migrans are frequently observed in toxocariasis, in which liver and lung may be involved. Thus, the aim is to investigate blood markers to differentiate among EGPA, HES, and toxocariasis.

Method: Four patients with EGPA, 6 patients with HES, and 16 patients with toxocariasis were included. Blood eosinophil counts, eosinophil cationic protein (ECP), total IgE, vitamin B12, and tryptase were compared between the different two diseases.

Results: Total IgE was lower in HES compared to EGPA ($P < 0.05$), although eosinophil counts, ECP, vitamin B12, and tryptase did not differ. Comparing EGPA with toxocariasis, eosinophil counts ($P < 0.05$) and ECP ($P < 0.05$) were higher in EGPA, with no differences in total IgE, tryptase, and vitamin B12. HES patients showed higher eosinophil counts ($P < 0.01$), ECP ($P < 0.01$), and vitamin B12 ($P < 0.05$) and lower total IgE ($P < 0.01$) compared to toxocariasis, with no difference in tryptase.

Conclusion: Based on our findings, total IgE and vitamin B12 levels may be additional markers to differentiate among EGPA, HES, and toxocariasis, in particular in cases of multiple organ involvements.

TP0740 | Cutaneous mastocytosis: A report of two cases

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Case report: Mastocytosis is a rare heterogeneous disease with a variable clinical spectrum of skin and systemic manifestations associated with the presence of an increased number of mast cells. The extent of mast cell proliferation, accumulation and degranulation determines the range of symptoms such as flushing, pruritus, hypotension, headache, diarrhea, vomiting, abdominal pain, syncope and anaphylaxis. In pediatric patients, skin involvement is more common and occurs in the form of solitary mastocytoma, diffuse skin mastocytosis (DCM), urticaria pigmentosa and telangiectasia macularis eruptiva perstans (TMEP). The clinical course of the disease depends on the age of the patient, the type of mastocytosis, the systemic involvement, the concomitant diseases and the response to the applied treatment.

We present two clinical cases: a 16-month-old boy with solitary mastocytoma and a 15-year-old boy with TMEP. The diagnosis was confirmed by skin biopsy. All of them presented with skin lesions within the first year of life. They also showed a positive Darier's sign. Both boys had frequent mast cell mediator-related symptoms such as itching, flushing, swelling, blistering, hypotensive episodes and dyspnea. Frequent exacerbation triggers included physical irritation and heat. Laboratory and genetic tests (KIT D816V marker) showed no abnormalities. Only the TMEP patient had elevated serum tryptase levels, interpreted as a potential indication for bone marrow biopsy. Patient treatment included oral antihistamines, sodium cromoglycate and topical medications. Regular follow-ups are performed. Furthermore, treatment response is monitored and adjusted accordingly.

SUNDAY, 2 JUNE 2019
TPS 08
ASTHMA: CLINICAL ASPECTS

TP0742 | Clinical phenotypes of severe asthma with fungal sensitization and treatment with biologics

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Background: Fungal sensitization (SAFS) represent a subtype of severe asthma often leading to a more severe outcome and potentially triggering the complex immune response of allergic bronchopulmonary aspergillosis. Both increased eosinophilia and perennial sensitization are in this contest recognized markers of eligibility for biologic agents.
Method: Retrospective data of 21 patients matching criteria for SAFS were collected among those followed in our severe asthma clinic according to difficult to treat and severe asthma GINA document. ABPA was excluded in all cases. Upper airways comorbidities, lung function, allergic sensitizations and treatments were analyzed in order to define the peculiarity of the phenotype in this subgroup of patients.
Results: The majority of patients were males (81%), mean age 60, with late onset asthma (85.7%) and often ex smokers (33.3%). Chronic rhinosinusitis was present in 81% with nasal polyps leading to surgery in 43%. Aspirin hypersensitivity was reported in 14.3% of cases. The median number of exacerbations was 2.4 /year and 66.6% of patients needed hospitalization, while the mean time of chronic systemic steroids intake was 5 years. Mean FEV1 and Tiffeneau index (TF) were 1.91 ± 0.20 and 57.6%±2.3 respectively; mean eosinophils count was 660.7 ± 97 cell/µl and mean total IgE was 758.1 ± 205 kUA/l. Monosensitization to molds was detected in 61.9% with a mean value of 2.03 ± 0.89 kUA/l. A significant higher number of exacerbations and worse degree of airway obstruction was detected in the monosensitized group compared to polysensitized (2.6 vs 1.7 respectively $P = 0.05$ TF 53.2 vs 64.2 $P = 0.045$ and FEV1 1.63 vs 2.35 L $P = 0.05$). Concomitant allergic sensitization to other inhalants was associated to higher total IgE, minor corticosteroid burden and increased TF (959 vs 356 kUA/l., $P = 0.04$; 6.6 vs 4.5 years $P = 0.039$ and 59.7 vs 53.2 l $P = 0.050$ respectively). 57.1% of patients were treated with omalizumab, 23.8% with mepolizumab and itraconazole was added in 57.1% of cases.
Conclusion: A significant disease severity in term of exacerbations, steroids burden, airflow obstruction and serologic markers within this cohort of SAFS patients is reported. Late onset, previous smoke habit and polyps comorbidity without aspirin hypersensitivity guess a peculiar disease history, while mould monosensitization and coexisting other allergen sensitizations could distinguish different phenotypes and suggest different response to biologics and antimycotic adjuvant treatment.

TP0743 | Early and late onset asthma in the elderly

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Background: Asthma associated morbimortality is higher in elderly patients. Adequate characterization of disease is important to achieve disease control. Early and late-onset asthma are widely used as phenotypic classifications, the former being more likely in atopic patients, presenting more frequently with acute exacerbations and having more severe fixed airway obstruction, and the latter presenting more commonly in female, obese and smokers. This study's goal is to compare major aspects of these two phenotypes in a population of elderly asthmatics.
Method: A retrospective study of patients with asthma diagnosis observed in our Asthma clinic between 2012 and 2016 was performed. Patients over 65 years old were divided into "early onset" and "late onset" groups, according to the age of diagnosis, and their data were statistically analysed.
Results: Out of the 86 patients included, 28 were classified as having "early onset asthma" and 54 as having "late onset asthma". In the first group, the majority of patients were women (75%; N = 21), 25% (N = 7) were current or former smokers and 32.1% (N = 9) were obese with a mean body mass index (BMI) of 34.3 kg/m^2 (sd 3.3). The most frequently found comorbidities were rhinitis in 21 patients (75%), gastroesophageal reflux disease (GERD) in 10 (35.7%), cardiac disease in 9 (32.1%), bronchiectasis in 7 (25%) and obstructive sleep apnea (OSA) in 3 (10.1%). Atopy was found in 39.3% of patients (N = 11). Mean FEV1 value was 75.5% (sd 25.9). Mean exacerbation number during follow up period was 0.8 (sd 0.7). In the second group, 61.1% (N = 33) were women, 20.3% (N = 11) had smoking history and 40.1% (N = 22) were obese and present with a mean BMI of 32.4 kg/m^2(sd 2.0). The most common comorbidity was rhinitis in 42 patients (77.8%), followed by GERD in 25 (46.3%), cardiac disease in 18 (33.3%), anxiety or depression in 9 (16.7%) and OSA in 6 (11.1%). Atopy was found in 51.8% of cases (N = 28). Mean FEV1 value was 84.1% (sd 23.4). Mean exacerbation number during follow up period was 0.6 (sd 0.6). A noteworthy difference regarding mean FEV1 value was identified (*P*-value 0.07).
Conclusion: Despite the lack of statistically significant differences, possibly due to small sample size, patients with early onset asthma presented with more severe fixed airway obstruction and had more exacerbations, whereas patients with late onset asthma were more frequently obese. Further studies are warranted to best characterize asthma phenotypes.

TP0744 | Seasonal alteration of isolated pathogens in children hospitalized with asthma exacerbation

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Background: Respiratory viral infections are associated with childhood asthma exacerbations. Most reports on viral infection associated with asthma exacerbation only evaluate one season. This study aimed to clarify the association between asthma exacerbation and causative pathogens in a single center over three seasons.

Method: Participants (n = 216) hospitalized with asthma between 2012 and 2015 (male: female, 134:82; median age, 3.4 years) were recruited. Nasopharyngeal mucosa cell samples were collected from the participants and examined by reverse transcription-polymerase chain reaction to amplify specific genes from rhinovirus (RV), respiratory syncytial virus (RSV), enterovirus D68 (EV-D68), parainfluenza virus (PIV), influenza virus, human metapneumovirus (hMPV), adenoviruses (AdV), human bocavirus (HBoV), coxsackie virus (Cox), and *Mycoplasma pneumoniae*. Clinical features, laboratory data, asthma exacerbation intensity, and asthma severity were compared among participants.

Results: Causative pathogens were observed in 171 participants. RV (64%) was the most commonly detected virus in the participants followed by RSV (6%) and PIV (4%). AdV (1%), EV-D68 (3%), hMPV (4%), and human coronavirus (2%) were also detected. The median age at admission in the RV group was significantly higher than that in the RSV or PIV groups. No significant differences were observed in clinical parameters between participants with RV type A and type C. There were 31 participants who were admitted repeatedly during the study period. RVs were detected equal to or greater than twice in 18 participants (58%) among them, whereas other viruses were not detected repeatedly in the participants. A small prevalence of EV-D68 was observed only in 2013.

Conclusion: Multiple year monitoring on causative pathogens is important to comprehend the prevalence of virus-induced asthma exacerbation.

TP0745 | Factors associated with low influenza and pneumococcal vaccination uptake in patients with severe asthma

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Background: Patients with asthma are susceptible to serious complications from influenza and pneumococcal infection. Vaccination for patients with asthma has been routinely recommended. In Slovenia vaccination for patients in risk groups is covered by national health insurance. The aim of our study was to find out the vaccination uptake in patients with severe asthma, and their behaviour concerning immunization.

Method: 104 severe asthma patients were asked about vaccination uptake in previous year. All of them were treated with asthma biologics. Those who were not vaccinated were further asked about reasons for this decision. A structured questionnaire was used to collect these data.

Results: The influenza vaccination rate among severe asthmatics was 19.2%. The most frequent reasons for not being vaccinated were lack of physician or nurse recommendation (23.75%), fear of side effects or sickness from the vaccination (18.75%), past experience of side effects (12.5%), and the belief that there is no need to be vaccinated. (12.5%). The pneumococcal vaccination rate was 8.7% only. Of all patients 23.7% did not know what this vaccine was for.

Conclusion: Influenza and pneumococcal vaccination uptake are very low within severe asthma patients. There is a lack of physician or nurse recommendation.

Health care professionals should take every opportunity for influenza and pneumococcal vaccination uptake advice. Communication strategies should focus on improving understanding and perception of personal risks arising from the disease and the importance and benefits of vaccination, as well as information regarding where, when and how to get the vaccine.

TP0746 | Adult asthma in a district hospital: A retrospective study

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Background: Asthma is a common chronic disease, estimated to affect around 339 million people worldwide. Its incidence has recently increased and it is responsible for a high burden of disability[1]. In Portugal the estimated prevalence of current asthma is 6.8%, with only 57% of patients having controlled asthma[2,3]. The aim of this study was to characterize the asthmatic population observed in our adult asthma clinic.

Method: Adults with asthma diagnosis observed in an asthma clinic at Hospital Beatriz Ângelo, between 2012 and 2016, were retrospectively analyzed.

Results: 624 patients were included. 70.6% were female, mean age was 44.8 ± 17.2 years and 93.3% were caucasian. Majority of non-smokers (66.7%). Mean BMI was 27.7 ± 5.4 kg/m2, 61% being overweight/obese. The diagnosis of asthma was made in childhood in 62.2% and in adulthood in 37.8%. The average follow-up time was 29.4 months. Just 37.3% maintained regular appointments. Asthma was severe in 41.3%, moderate in 35.4% and mild in 22%. Median

number of exacerbations per year of follow up was 0.4 (IQR 0 to 0.93), with a total of 59 patients with hospital admissions for asthma exacerbations in the observed period. Asthma was controlled (Asthma Control Test [ACT]) > 19), in the last evaluation, in 90.1% of patients.

In terms of comorbidities: 84.8% had rhinitis, 25.6% gastroesophageal reflux disease and 10.9% had a diagnosis of anxiety/depression. 47.9% had evidence of atopy. Mean FEV1 was 87.2 ± 19.1%. 18.9% with a positive methacholine test. 5.3% performed a cardiopulmonary exercise testing. Most of the patients (84.5%) were treated with an inhaled corticoid, 73% with concomitant long-acting β2-agonists (LABA), 41.8% with montelukast and 8.8% with long-acting muscarinic antagonists (LAMA). 70.4% were doing a nasal corticoid and 69.7% an anti-histaminic. Just 2 patients were on long term oral corticoids and 3 with biologic therapy. 13.5% of patients had a history of immunotherapy.

Conclusion: Despite the high prevalence of overweight/obese patients and rhinitis in our population, good asthma control was achieved in the majority. Most patients included in this study had severe asthma, probably because less severe patients are less often sent to our clinic. Nevertheless, abandonment rate was high and most patients were lost for follow-up. Careful analysis of the characteristics of our asthma patients allows us to develop better tools to improve can follow up, tailor our therapeutic strategies and obtain better patient adherence.

TP0747 | Asthma may increase the risk of non small cell carcinoma

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Background: Evidence has shown that asthma may increase the risk of lung cancer. However, which cell type of lung cancer (small cell carcinoma of the lung(SCLC) or non SCLC) was associated with asthma remains unknown. We conducted a nationwide cohort study to evaluate which cell type of lung cancer was associated with asthma.

Method: Lung cancer cohort cases from National health insurance research database were separated into SCLC and non SCLC. Controls were and were matched by age, gender and date of LC diagnosis at a ratio of 1:4. Information was collected 8 years prior to diagnosis of LC. We used conditional logistic regression to evaluate the trend of developing lung cancer. Further, we stratified all subjects into SCLC and non SCLC groups and adjusted for age, gender and comorbidities.

Results: Patients who had asthma for at least 2 years had an odds ratio of 1.70, which increased to 2.30 for patients who had asthma for over 6 years. After stratification LC cohort into SCLC and non-SCLC, we found SCLC was most prevalent in the 60-80 age group(61.81%) and in males(90.42%). However, these was lower in the non-SCLC group with prevalence(53.31%) and males(61.91%). Patients with asthma had lower risk of developing SCLC than non-SCLC while length of asthma history did not. The risk of developing non-SCLC increased as the length of asthma history increased ng cancer. Further, we stratified all subjects into SCLC and non SCLC groups and adjusted for age, gender and comorbidities.

Conclusion: Asthma is associated with an increase risk for non-SCLC. The risk of developing lung cancer increased as the length of asthma history increased.

	CONTROL N = 67, 076	Lung cancer N = 16, 769	OR
Asthma history			
Without			1(ref.)
>2 year	1252	606	1.70*
>3 year	1106	553	1.76*
>4 year	967	508	1.87*
>5 year	801	450	2.02*
>6 year	635	397	2.30*

* Adjust: Age, Comorbidities.

TP0748 | Risk of periodontal disease in patients with chronic respiratory disease: A nationwide population-based cohort study

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Background: The asthma has a great impact on many aspects, such as mental disorder, quality of life and social economic burden, including oral health. In addition to caries, periodontal disease is the most prevalent oral disease among adults in the world. Both asthma and periodontal disease are chronic inflammatory disorder. Previous studies indicate that children and adults with asthma have more gingivitis and periodontal disease compared to non-asthma patient. The

aim of the study was to evaluate whether patients with asthma have an increased risk of developing periodontal diseases than controls and compare the differences which was stratified by age and sex. Also, we want to know whether patient with asthma receiving periodontal therapy can reduce the frequency of exacerbation.

Method: We used the National Health Insurance (NHI) of claim data in Taiwan to evaluate the risk of periodontal disease in asthmatic patient. This study used the Longitudinal Health Insurance Database 2005(LHID2005), a subset of claims data of NHIRD, obtained from the NHI, consisting of claims data of one million randomly selected NHI enrollees. We selected newly diagnosed patients with asthma, from 1997 through 2012 identified and included in the asthma cohort. Patients with history of periodontal disease were excluded. To avoid immortal time bias, the comparison cohort was selected by using time-dependent analysis. Both cohorts were followed from the index date until diagnosis of periodontal disease occurred, death or the end of the year in 2013, whichever came first.

Results: 15 414 patients (7237 males and 8177 females, respectively) with newly-diagnosed asthma were enrolled from the 1997-2012 database. The mean age±SD for asthma group was 49.18 ± 13.83. After adjusting potential confounding factors by Cox regression model, our results demonstrated that incidence of periodontal diseases significantly increase in the asthma cohort than the comparison cohort ($P < 0.01$). In addition, the frequencies of asthma exacerbation became significantly lower after receiving periodontal therapy than controls ($P < 0.01$).

Conclusion: Our finding suggested that asthma was associated with increasing risk of periodontal disease. Receiving periodontal treatment in asthmatic patient may improve exacerbation frequency. Thus, patient with asthma should be aware of their oral hygiene to prevent asthma exacerbation.

TP0749 | Evaluation of the risk of developing thromboembolic events in patients with bronchial asthma

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Background: The involvement of coagulation in the path physiology of asthma has recently been implicated. Bronchial asthma is associated with a local activation of coagulation and could be increased by the use of medication for its treatment and severity. Therefore, asthmatic patients would have an increased risk of pulmonary y embolism.

Method: Descriptive, prospective cross-sectional study. 74 patients participated, between 6 and 75 years of age with a diagnosis of bronchial asthma, who attended the Department of Allergy and Immunology and the Department of Pneumology and immunology, in the period of March 1 from 2018 to July 30, 2018.

Results: The effects of SABA on coagulation in asthmatic patients expresses that 17.24% presented alteration in coagulation. As for OCS, it is not significant and represents 2.3% (p: 0, 85). Regarding antileukotriene there is no risk of developing a prothrombotic event (p: 0, 65). In the case of ICS (p: 0, 98), 3.3% of the budesonide plus formoterol combination had their parameters altered. It is inferred that exclusive budesonide at low doses, only affects 3.3% of patients. The same is evident for patients medicated with fluticasone plus salmeterol. In the case of pediatric patients, only one presented altered parameters and it was not significant. 16.27% of adult patients presented a prothrombotic state, in the case of pediatric patients it was 3.2%.

Conclusion: In the case of the adult population, the prothrombotic state is directly associated with the severity of bronchial asthma. The medication does not affect the coagulation of patients with bronchial asthma since the percentages are not significant. Regarding the pediatric population, the results express that the prothrombotic state is not associated with the severity of bronchial asthma, no association with coagulation and medication was found.

TP0750 | The interaction effect between early cigarette smoke and early-onset asthma on the risk of mental illness

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Background: Children with asthma increase their risk of mental illness during childhood and adolescence. One prospective study using the Taiwan National Health Insurance Research Database (NHIRD) found that adolescents with asthma had a higher incidence of mood disorders in later life. Another study found that well-controlled asthmatic children do not increase the prevalence of depression and anxiety. Previous studies have suggested that asthma symptoms are increased in cigarette smokers and smoking may increase the risk of anxiety during late adolescence and early adulthood. The aim of this study was to test the association between cigarette smoke, asthma, and mental disorders in a large population-based follow-up study.

Method: The participants (N = 170 457) were students aged 11-16 years old from 123 high schools in the Kaohsiung and Pingtung regions from 1995-1996. Through linkage with NHIRD, 6539 newly-diagnosed asthma patients and 143 293 non- asthma were identified in 1999-2014. This cohort was followed-up for five common mental diseases, including panic, bipolar, anxiety disorders, major depression and any depression disorder until December 31, 2015. According to the age at onset of asthma, we divided patients into two groups: early-onset asthma (<20 years) and late-onset asthma (≥20 years). Cox proportional hazard model was used to analyze the Hazard Ratio (HR) of mental disorders on asthma after adjusting for gender, age, residence, parent education level, prednisone

use, allergic comorbidities, Charlson comorbidity index and cigarette smoking behavior.

Results: Asthma patients was associated with higher risk of panic disorder (HR: 1.70, 95% CI: 1.28-2.26), bipolar disorder (HR: 1.31, 95% CI: 1.12-1.53) and anxiety disorder (HR: 1.35, 95% CI: 1.15-1.58) than non- asthma subjects. Compared to non-smokers with non-asthma, current smokers with early-onset asthma revealed stronger effects on panic (HR: 4.95, 95% CI: 1.23-19.9), bipolar (HR: 3.10, 95% CI: 1.29-7.44) and anxiety (HR: 3.34, 95% CI: 1.39-8.06) disorder.

Conclusion: Our results suggested that asthma was associated with increased risk for mental illness. In addition, early-onset asthma patients and smoking have a strong interaction effect on mental disease. Therefore, smoking cessation and good control of asthma may helpful in reducing the risk of psychiatric disorders.

TP0751 | Bronchial asthma and scleroderma

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Background: We investigated some clinical and immunological parameters in 11 patients with systemic scleroderma and bronchial asthma, preceding at least 3 years of systemic scleroderma.

Method: We followed the 11 patients with bronchial asthma and systemic scleroderma including 10 women and 1 men, Caucasian type, aged 41 to 80 years, with diseases duration of 5 to 20 years. The study is open and multi-center. Were examined following indicators: Bronchodilator test whit Spirometry, Peak flowmetry, X-ray change, biopsy, Doppler sonography, capillary in the area of the nail fold of the fingers, Anti-SCL-70 antibodies, CRP, ANA, Anticentromeric antibodies, levels complement and other.

Results: All patients completed the study. In all patients, X-ray change - pulmonary fibrosis and emphysema is observed in all at varying degrees of development. All patients report more frequent and severe respiratory infections after the development of scleroderma for a longer recovery period and objectively reduced breathing parameters /reported by daily two-fold peak flowmetry/ crisis with leukoclastic infiltration in 10 patients and lymphocyte infiltration in 1 and collagen accumulation. All patients have performed capillaroscopy and Doppler sonography are established complete arterial obstruction, in 2 patients with peripheral gangrene, and incomplete in 4 patients, accompanied by tingling of the fingers. Trophic ulcers the toe tips, such as “rat bite”, were observed in 6 patients (54, 5%).Fibrosis of the skin of the fingers often leads to flexion contractions, which we observed in 6 patients. We were watching two-sided swelling of the fingers, but it was very pronounced in 5 patients (45, 5%). 10 of our patients have impaired motility of the esophagus. Accelerated ESR and C-reactive protein were found in 5 patients as follows - 2 intensively accelerated and 3 moderate. In our patients with positive ANA, we observed 4 patients - at low titer 1:40 at 2 and titration 1:80 in 2 patients. We underline the importance of ANA (57%) and anti-CC antibodies (27%) for the early diagnosis of Raynaud's syndrome and scleroderma, which is also seen in our patients. Anti-SCL-70 antibodies were observed in 3 patients coinciding with other publications describing about 40% of the patients. Low levels of complement were observed in 2 patients. Low hemoglobin levels were observed in 1 patient, with no iron deficiency.

Conclusion: Scleroderma, coupled with pulmonary fibrosis, aggravates the symptoms of bronchial asthma.

TP0752 | Bronchial asthma and pulmonary tuberculosis as comorbid diseases

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Background: Objective. Determine the frequency of the presence of bronchial asthma in patients with pulmonary tuberculosis (TB), its structure and the effect on the results of treatment of patients with TB.

Method: Case reports of 2053 TB patients aged 20-60 years with newly diagnosed TB were analysed. For the diagnosis of asthma and TB, clinical and anamnestic data, x-ray, microbiological, spirometric, and skin and laboratory testing data with allergens were used.

Results: The frequency of asthma in patients with newly diagnosed TB in 2008-2017 averaged 5.4%, with fluctuations by year within 2.8%-7.3% of cases. At the same time, intermittent asthma occurred in 27 (24.5%) people, persistent mild - in 36 (32.7%) patients, persistent moderate - in 28 (25.5%) patients, persistent severe - in 19 (17, 3%) people. Cavity destruction somewhat more frequently (by 7%) occurred in patients with asthma. However, among patients with asthma with exacerbation of it and without it, the proportion of persons with bacterial excretion was approximately the same (51.2% versus 48.8% of cases).

In the presence of asthma and TB comorbidity, especially if control over its course was lost as a result of exacerbation, it was logical to expect a negative effect of asthma on the results of treatment of TB patients. Exacerbations in patients with newly diagnosed TB slowed down the cessation of bacteria excretion (after 2 months of treatment, sputum negativity was observed in 74.3 + 4.7% of people without exacerbations of asthma versus 60.2 + 5.6% with their presence, $P < 0.05$) and healing of cavities of destruction in the lungs (after 3 months of treatment in patients without asthma exacerbations, cicatrization of destruction was observed in 44.6 + 6.7% of persons versus 25.3 + 3.8% of those examined with exacerbations, $P < 0.05$).

Conclusion: Asthma and TB meet the criteria for comorbid disease. Exacerbations of asthma adversely affect the results of treatment of

patients with TB, slowing down the timing of the cessation of bacterial excretion and scarring of the cavities of destruction in the lungs. This combination is an important medical and social problem that requires further study and development of appropriate measures aimed at timely diagnosis, effective treatment, prevention of development and further progression of both diseases.

TP0753 | Asthma and obstructive sleep apnea

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Background: There is growing evidence that patients with asthma have a higher prevalence of obstructive sleep apnea (OSA). Previous studies focus mainly on OSA screening in uncontrolled asthmatics.[1,2] The aim of this study was to investigate the prevalence and characteristics of the overlap syndrome "asthma and OSA" in our population.
Method: Retrospective analysis of patients observed in our Asthma Clinic between 2012 and 2016 with asthma diagnosis who performed a sleep study.
Results: 55 patients were included. OSA was diagnosed in 85.5% (47 patients). Cardiorespiratory polygraphy was performed in 69% and polysomnography in 31%. Mean age was 57.3 ± 13.1 years. 53.2% were females. Mean BMI was 33 ± 5 kg/m^2 and 72.3% were obese. Asthma was severe in 55.3%, moderate in 29.8% and mild in 14.9%. Asthma was controlled (Asthma Control Test [ACT]) > 19) in 84%. Spirometry showed obstruction in 53.3% and was normal in 46.7%. Mean Epworth Sleepiness Scale (ESS) score was 10.5 ± 6.3. Snoring was present in 92.7%, nonrepairing sleep in 78.4%, witnessed apneas in 41.7%, morning headaches in 29.4% and gasping in 14.3%. Mean AHI (apnea—hypopnea index) was 22.5 ± 16.6 respiratory events per hour. OSA was mild (AHI 5-14.9) in 44.2%, moderate (AHI 15-29.9) in 27.9% and severe (AHI ≥ 30) in 27.9%. Positive airway pressure therapy was initiated in 76.6% and 69.4% of these were adherent. There was no significant improvement in ACT after initiation of PAP therapy.
Conclusion: OSA is highly common in asthmatics even if their disease is controlled. Therefore, screening for OSA is important not only in poorly controlled asthma but in all asthmatics especially those with OSA symptoms. Absence of ACT improvement with PAP therapy in this population might be related to high asthma control rate at baseline.

TP0754 | Respiratory function features in pregnant women suffering from bronchial asthma

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Background: The treatment of women with bronchial asthma during pregnancy is the treatment of both the mother and the unborn child, to the volume and content of which increased demands are made. The goal of our study was to reveal changes of external respiratory function during pregnancy, most reflecting the subjective and objective manifestations of bronchial obstruction.
Method: Within our survey 1010 pregnant women who noted signs of reversible bronchial obstruction were examined with the use of body plethysmography and spirometry methods by MasterScreen Body (ERICH JAEGER, Germany).
Results: It was shown that the forced expiratory volume can remain within the framework of normal values even in patients with moderate persistent asthma. Decrease of FEF50, increase of airway resistance (Raw) and decrease of specific airway conductance (sGaw) correlated most clearly with the severity of disease symptoms. The initial level of FEF50 as well as the increase of this parameter in the test with b2-agonist correlated with the severity of bronchial asthma. In 28% of patients who had no complaints were detected auscultative signs of bronchial obstruction. In this group there were significant differences of FEF50 (P = 0.014) and Raw (P = 0.029) with the group where were no auscultative signs of bronchial obstruction.
Conclusion: When prescribing therapy to pregnant women suffering from bronchial asthma, subjective, objective signs of bronchial obstruction as well as instrumental survey data should be taken into account.

TP0755 | Relationship between asthma and sarcopenia in the elderly population: A nationwide cross-sectional study from KNHANES 2008-2011

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Background: The prevalence of asthma has been greatly increasing in the older population in recent years. With the previous study showing that regular physical activity was important for healthy aging, physical activity plays potential roles on healthy aging, and lowering the risk of development of several diseases, there has been no study on the relationships of asthma with that including physical activity. Therefore, we aimed to examine the relationships of asthma with sarcopenia including physical activity in a nationwide population.
Method: A cross-sectional dataset from 28 758 participants in the Korean National Health and Nutrition Examination Survey 2008-2011 was analyzed. History of asthma, including asthma onset age, recent asthma exacerbation, and hospitalization due to asthma exacerbation was asked using structured questionnaires. Appendicular skeletal muscle was calculated as the sum of the skeletal muscle mass, and physical activity was calculated as

metabolic equivalents by using the International Physical Activity Questionnaire.

Results: Estimated proportion of asthma patients was 6.17 ± 0.37% in the elderly, and those were older, female predominant, more obese, lower lung function, and myopenia than never asthma. Asthma with myopenia was significantly related to older age, younger asthma onset age, male predominance, less obese, lower lung functions, and lower physical activity, and had a higher proportion of admission and recent asthma exacerbation (vs asthma with non-myopenia). However, sarcopenic asthma, which is myopenia with lower physical activity, were not significantly associated with lower lung functions, and asthma exacerbations compared to that with moderate or high physical activity.

Conclusion: Although asthma with myopenia had lower lung functions, a higher proportion of asthma exacerbation, and lower physical activity, sarcopenia was not related to lung functions and asthma controls in the community elderly population. Therefore, muscle mass may play a more important role in lung functions and asthma controls than physical activity.

TP0756 | Respiratory food allergy: A pilot study

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Background: The role of diet in the etiology of asthma has become a popular research in recent years and a strong association between food and respiratory allergy has been reported. Food sensitization, affects both local and systemic markers of inflammation in asthma and particularly IgE sensitization to egg has been known as a risk factor for aeroallergen sensitization and asthma later in life. However, the role of non-IgE mediated food allergy and the most common one :cow's milk food allergy,in triggering asthma has been less investigated. The aim of this study was to determine the relationship between non- IgE mediated cow's milk allergy and hard-to-treat asthma.

Method: All children up to 12 years of age who had been initially referred as asthma not responding to a 2 week of a standard treatment and paying special attention to comorbid conditions were enrolled in the study. Evaluation was according to Asthma Control Test. Dietary avoidance from cow's milk protein was recommended for another 2 weeks along with asthma conventional therapy.

Results: 71 patients completed the study, of whom more than 50% of the patients were between 5 and 10 years of age. 58% of the patients were female and 42% were male. More than 82% of the patients in this study with hard-to-treat asthma responded to an elimination diet and their Asthma Score Test was improved.

Conclusion: To conclude, non-IgE-mediated food allergy with cow's milk protein as a prototypic major food allergen may play an important role in difficult-to-treat childhood asthma. Food avoidance is recommended as a suitable diagnostic and therapeutic tool for non-IgE-mediated food allergies. The high rate of therapeutic effects of this approach in the children in this study, suggests a valuable role for this approach in the treatment of refractory asthma in children.

TP0757 | Allergic bronchopulmonary aspergillosis as a complication of COPD: A new entity

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Background: Allergic broncho-pulmonary aspergillosis (ABPA) is associated with two recognized conditions: asthma and cystic fibrosis. Here, we report on patients with ABPA occurring in patients with long-standing chronic obstructive pulmonary disease (COPD)

Method: Adult patients with diagnoses of both COPD (GOLD criteria) and ABPA (Patterson's criteria) followed in our institution were identified thanks to the medical information system database. Patients' demographic, clinical and paraclinical (including spirometry values and assessment of Bhalla scoring system on chest CT-scans) findings as well as follow-up outcomes were recorded and compared to 16 ABPA-free COPD patients matched on age, FEV1 and follow-up duration.

Results: 16 patients (13 men), median age (IQR) 61 years (ranging from 55 to 79 years), median tobacco consumption 47 PY were identified. The diagnosis of ABPA followed that of COPD after a median of 6 years (with a range from 1 to 10 years). At diagnosis of ABPA, median FEV1 was 36% (1127 mL). All patients were investigated for specific IgE = 19.4 kUI/l, IgE = 2684 kUI/l, eosinophilia = 1271/mm3. 13/16 had positive IgG, 10 had evidence of *Aspergillus sp.* in sputum. Immediate prick tests were positive in 6 out of 7 patients. All patients received inhaled and oral steroids, 13 patients received oral fungicides and 7 omalizumab.

During follow-up, annual rate of FEV1 decline (-56 vs -34 mL/year; $P = 0.04$) and hospitalization rates for flare up (1.69 vs 0.53/year; $P = 0.0007$) were significantly higher in ABPA-BPCO patients than in ABPA-free COPD patients. Bronchiectasis extension ($P = 0.002$) and mucoid impaction extension ($P = 0.03$) but not emphysema ($P = 0.45$) were significantly higher in ABPA-BPCO patients than in ABPA-free COPD patients. Among ABPA-BPCO patients, the use of antifungal drugs prevented the loss of FEV1 (-51 mL/year vs + 92 mL/year; $P = 0.02$) whereas omalizumab tended to lower the annual exacerbations rate.

Conclusion: ABPA can occur during the course of COPD and is associated with impaired respiratory function and multiple hospitalizations. Treatment with antifungal drugs and/or omalizumab could improve long-term outcomes and should be discussed promptly once the diagnosis is established.

TP0758 | Association between asthma control level and degree of anxiety in adult patients

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Background: Psychiatric disorders occur frequently in the general population. The most common are anxiety disorders (14%) and mood disorders (7.8%); It has been observed that psychiatric comorbidities are more common in patients who have chronic somatic diseases, such as in patients with respiratory diseases such as Asthma and Chronic Obstructive Pulmonary Disease. Objective: To establish the association between the level of asthma control and the degree of anxiety in adult patients.

Method: Design, observational, transversal and analytical. In adult patients with asthma. Collection of demographic data, stratification of the level of control of Asthma according to international criteria was performed, as well as Spirometry performed with personnel with NIOSH certification, and application of the Beck Anxiety Inventory, validated in Mexico.

Sample size calculation: with the formula for proportion differences, considering IC 95%, 226 patients. The statistical analysis was performed depending on the type of variable used.

Results: 204 patients, 59.8% women and 40.2% men. 50% with controlled asthma, 34.7% partially controlled asthma and 16. 7% uncontrolled asthma. 77.5% of patients with Anxiety, of which 41.5% with mild anxiety. Multiple logistic regression model, to predict Anxiety, adjusted for female sex, onset of bronchial symptoms > 5 years, presence of obstructive pattern, and uncontrolled asthma with a correlation coefficient of 20.6%.

Conclusion: The prevalence of anxiety in patients with asthma was higher than reported in the literature (77.5 vs 34.7%). The factors that influence the development of anxiety in patients with asthma are multiple and lack of control of the disease is a very important factor.

TP0759 | Bronchiectasis in severe asthma, a distinct clinical profile

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Background: Asthma and bronchiectasis (BE) are two heterogeneous diseases that frequently coexist, particularly in severe asthma (SA). Previous studies in asthma with BE have included inhomogeneous populations, resulting in inconsistent outcomes. Studies in truly severe refractory asthma, according to the current international guidelines, are lacking.

We hypothesize that BE contribute to asthma severity and patients with SA and BE present themselves with more severe illness compared to SA patients without BE.

Method: A single centre, retrospective observational study of adult patients with SA consecutively recruited from a tertiary referral centre in The Netherlands. SA was confirmed, after a systemic assessment with a multidisciplinary approach, using the ATS/ERS guidelines. Two independent radiologists blinded to the other research findings, evaluated each Computed Tomography (CT) using the modified Reiff score.

Results: A total of 105 patients with SA (<15 PY) were included. In 91 (87%) patients a CT was available. 19% of patients with SA showed BE on CT. Patients with BE had a lower FEV1% predicted (63.94 ± 16.86 vs 76.18 ± 19.95; $P = 0.02$) and FEV1/FVC (57.22 ± 10.29 vs 66.35 ± 11.82; $P < 0.01$). There was a non-significant trend towards more hospitalizations in the group of patients with SA and BE (1.41 ± 1.70 vs 0.77 ± 1.05). The number of infectious exacerbations/antibiotic cycles was significantly higher in the group of patients with SA and BE (1.53 ± 1.46 vs 0.50 ± 0.85). Notably both groups showed elevated mean blood eosinophil levels with slightly higher levels in patients with SA and BE (0.85 ± 0.52 vs 0.56 ± 0.48; $P = 0.03$). Sensitization to *A. fumigatus* was found in 53% of BE patients and in 20% of non-BE patients. 88.2% of patients with SA and BE had one or more positive sputum cultures compared to 36.5% of patients without BE($P < 0.001$). A longer duration of asthma and older age were associated with the existence of BE.

Conclusion: In an extensively characterized, well defined, SA cohort, the prevalence of BE is 19%. The presence of BE in SA is associated with worse lung function, more infectious exacerbations and higher blood eosinophils. BE are more common in SA patients with a longer duration of asthma, older age at presentation, sensitization to *A. fumigatus* or a positive sputum culture. These results can possibly contribute to early recognition of BE in SA.

TP0760 | Two cases of adult asthma patients suffered from repeated pneumonia due to inhaled corticosteroid

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Case report: Inhaled corticosteroid (ICS) is the first-line medicine and essential for asthma treatment. The side effects for ICS are rarely manifested. However, increased risk of infection is thought to be one of the side effects for ICS. We experienced two cases of asthma patients who suffered from pneumonia several times due to ICS treatment.

Case 1: A 46-year-old man. His onset of asthma was at the age of 35. He was treated with fluticasone propionate/salmeterol, montelukast, and epinastine. He suffered from pneumonia in the right lower lobe, at the age of 40. He was treated with antimicrobial medicine. In Computed Tomography (CT) after the treatment, finding of pneumonia was improved. After that, he suffered from pneumonia and hospitalized for treatment twice. He also often suffered from respiratory infection, and needed to take antimicrobial medicine. Then, he was introduced to our hospital at the age of 42. At that time, he stopped taking ICS (fluticasone propionate) and treated only with montelukast and epinastine. Finally, he did not suffer from pneumonia, under the well asthma controlled.

Case 2: A 53-year-old women. Her onset of asthma was at the age of 40. She was treated with fluticasone propionate/salmeterol and montelukast. She suffered from pneumonia twice and treated with antimicrobial medicine. Then, she was introduced to our hospital at the age of 50. At that time, fluticasone propionate/salmeterol was changed to budesonide/formoterol. Even though, she still suffered from pneumonia twice, and needed to take antimicrobial medicine. After that, she stopped taking ICS (budesonide) and treated only with montelukast. Then, she did not suffer from pneumonia, under the well asthma controlled.

We reported two cases of adult asthma patients who repeated pneumonia, and ceased it by discontinuing ICS treatment. However, there is also a concern that asthma control may deteriorate when we discontinue the ICS treatment. So we need to accumulate the cases and clarify the characteristics of patients who have increased the risk of infection by ICS treatment.

TP0761 | Persistent rhinitis and asthma due to ferret's allergy

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Case report:

Background: The prevalence of exotic pet allergies has been increasing in recent years. The ferret (*Mustela putorius*) is the domesticated form of the European polecat, a mammal belonging to the same genus as the weasel. The allergic symptoms are mainly respiratory (rinitis, conjunctivitis and asthma), although contact urticaria has also been reported.

Case report: We report the case of an 18 year-old female who has a 4 years history of rhinoconjunctivitis and asthma that started after the adoption of a male ferret. She needs oral antihistamines and inhaled corticosteroid and long acting beta agonists daily, and refuses to remove the ferret from home. Skin prick test (SPT) were positive to ferret, cat, dog, rabbit, cypress and grass pollens. The ferret SPT was performed with ferret's lyophilized dander diluted in PBS (3 mg/mL) and the wheal diameter was 10 mm. Ferret specific serum IgE (ImmunoCAP) was 2.38 kUA/l. Total IgE was 216 kU/l. An IgE immunoblot was performed with the ferret extract and several IgE binding bands were identified at 66 KDa (probably serum albumin, already described as allergen in ferret), and at (approximately) 21, 17, 14 and 13 KDa. The latter 4 bands have not been described previously as ferret allergens, and may correspond to lipocalins.

Conclusion: We present a case of persistent moderate allergic rhinitis and asthma due to ferret. Allergy to exotic pets should be ruled out in owners with persistent respiratory symptoms.

Key words: ferret, asthma, new allergens, lipocalins, uncommon pets

TP0762 | Montelukast - an unknown cause of acute fibrinous organizing pneumonia (AFOP)

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Case report:

Introduction: Montelukast is an antagonist of leukotriene receptors indicated for the treatment of asthma and rhinitis. There have been some associations of montelukast to eosinophilia and vasculitis, but there are no reports of its association with AFOP.

Clinical Case: A 40-year-old female, smoker, with a medical history of asthma, diabetes mellitus and dyslipidemia, chronically medicated with salmeterol + fluticasone (500 + 50 ug), salbutamol SOS, metformin, simvastatin and alprazolam, has initiated follow-up in a pneumology outpatient clinic due to uncontrolled asthma with frequent exacerbations. She stopped the previous inhaler and started on Formoterol + Budesonide (320 + 9 ug) 3 times daily and montelukast.

The patient showed clinical improvement in the first month of treatment, followed by a new clinical worsening with dyspnea and wheezing, without signs of respiratory infection. No other medication was started.

Analytically presented with 1180 eosinophils/uL (10.6%) (not present in previous analytical studies), positive Phadiatop, negative ANCA, ANA, serology for Aspergillus and parasitological examination of feces.

Pulmonary function test showed a slight restrictive ventilatory pattern. Thoracic CT scan revealed multiple bilateral nodular ground-glass densifications (the largest one with approximately 9 mm).

She underwent a bronchofibroscopy that showed no structural changes and no microbiological identification. In the bronchoalveolar lavage, a discrete eosinophilia (2.4%)was identified.

Given the inconclusive results, the patient underwent a transthoracic biopsy guided by CT where was verified an improvement of the previous lesions but with new ground-glass lesions. Histological findings suggested Eosinophilic Pneumonia vs AFOP. During the

diagnostic investigation the patient had self-suspended montelukast due to a skin rash that she thought to be related with the medication. After suspension of montelukast, it was observed the resolution of the peripheral eosinophilia and radiological changes, without the need for systemic corticosteroid therapy.

Conclusion: Clinical findings suggested montelukast as a cause of AFOP since other eventual causes were excluded and improvement occurred after withdrawal of montelukast. Radiological findings not suggesting Eosinophilic Pneumonia and the eosinophils < 25% in BAL allowed to exclude this diagnosis. Of the best of authors knowledge this is the first case of AFOP related to montelukast.

SUNDAY, 2 JUNE 2019
TPS 09
THE WIDER WORLD: NOVEL DIAGNOSTICS AND QUALITY CARE

TP0764 | Two-site immunoassays for the quantification of major egg allergens ovomucoid (Gal D 1) and ovalbumin (Gal D 2)

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Background: Hen's egg is one of the most common causes of food allergic reactions. Of those who are sensitised, the majority produce an IgE response to Ovomucoid (Gal d 1) and Ovalbumin (Gal d 2). Accurate measurement of Gal d 1 and Gal d 2 is important for numerous applications, including standardisation of allergen products, quality control during egg-derived vaccine production, as well as food and drink quality control. Our aim was to develop highly sensitive and specific two-site immunoassays for the quantification of major egg-allergens Gal d 1 and Gal d 2.

Method: Natural Gal d 1 and Gal d 2 were purified from partially purified egg extracts and used to immunise mice for monoclonal antibody development. Antibodies were screened and suitable pairs identified to develop two-site ELISAs against Gal d 1 and Gal d 2. Samples including diagnostic and therapeutic products, egg-derived vaccines and foods were analysed using the assays.

Results: Both Gal d 1 and Gal d 2 assays were sensitive; each respectively having a lower detection limit of 7.81 ng/mL and 0.39 ng/mL. Assay accuracy and reliability was also strong, with recovery being ± 30% as well as intra and inter-assay variability < 15%. Specificity testing revealed the assays reacted specifically to their target egg allergen. Egg allergens Gal d 1 and Gal d 2 were quantified in diagnostic and therapeutic products, egg-derived vaccines and foods.

Conclusion: We generated highly sensitive and allergen-specific two-site ELISAs for the quantification of major egg allergens Ovomucoid (Gal d 1) and Ovalbumin (Gal d 2). The assays developed have applications in measuring egg allergens in therapeutic and diagnostic preparations, quality control of egg-derived vaccines, egg-white derived fining agents in wine and food quality control.

TP0765 | Do hypoallergenic horses exist? Comparison of Equ C 4 levels in dander from ten horse breeds

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Background: Horses are valued by many people in sport, leisure and healthcare. Horse-allergic individuals are limited in their ability to interact with horses. To meet their needs, the existence of hypoallergenic horse breeds has been suggested. This is mainly based on anecdotal evidence of higher tolerance to certain horse breeds, such as the Russian Bashkir horse. The objective of this study was to compare levels of the horse allergen Equ c 4 in dander from ten horse breeds. The latherin protein Equ c 4 has a function in the thermoregulation of equines.

Method: The study population included 170 horses (87 mares, 27 stallions, 56 geldings) from ten breeds: American Curly (AC), American Quarter horse (AQ), Gotland Pony (G), Icelandic horse (I), North Swedish horse (N), Russian Bashkir horse (B), Shetland pony (SP), Standardbred (S) and Swedish Warmblood (SWB). Horse dander was collected by grooming the horses over the whole body. Levels of horse allergen Equ c 4 were quantified using a two-site sandwich ELISA with mAb 103 and 14G4 and the protein content was analysed using the Pierce™ BCA Protein Assay Kit. The results were expressed as Equ c 4 U/µg protein.

Results: The horse allergen Equ c 4 was detected in all dander samples from the ten horse breeds, with high within-breed and inter-breed variations. The geometric mean values were 639 with a range of 5-15264 Equ c 4 U /µg protein. No differences between breeds could be seen, adjusted for age, sex and changes over time. The levels were significantly higher in samples from stallions compared to mares and geldings, independent of breed.

Conclusion: The results show a high within- and between breeds variability in levels of Equ c 4. Significantly higher levels were found in stallions compared to mares and geldings, independent of breed. Results show no scientific evidence for a hypoallergenic horse breed, since all ten horse breeds had Equ c 4 levels and therefore cannot be recommended for individuals allergic to Equ c 4.

TP0766 | Adherence to the STROBE checklist in articles published in EAACI journals: A systematic review

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Background: Reporting guidelines have been a tool for improving written scientific communication in form of published articles for almost two decades. Prior studies show that the reporting quality of observational studies is still suboptimal after publication of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline in 2007. This systematic review aims to determine to what extent articles published in EAACI Journals (Allergy, PAI, CTA) adhere to each item in the STROBE guideline.

Method: We searched PubMed for articles of observational studies published in the three EAACI journals between 2009 and 2017. We randomly choose ten articles per year of each journal. Currently, one rater (EW) evaluates each of the included articles using the STROBE checklist. Up to now, five randomly chosen articles have been evaluated by a second rater (JG).

Results: From a total of currently 259 selected articles (39% cohort, 20% case-control, 41% cross-sectional studies), we have so far evaluated 107 articles. Among these, all provide a balanced summary in their abstracts as well as a rationale. However, 11% did not report location and relevant dates of the study and a further 33% lacked some information on basic study setting characteristics. Only 23% fully described methods to control for confounding and further 23% at least mentioned employed methods without detailed description. Handling of missing data was described in 21% of the articles. Almost all studies described key results in their discussion section and 69% discussed study limitations in detail.

Conclusion: Our results show suboptimal reporting quality of observational studies published in *Allergy*, *Pediatric Allergy and Immunology*, and *Clinical Translation Allergy* from 2009 to 2017. Some characteristics which can be described using few words only are neglected in a substantial portion of evaluated articles. Other characteristics may require more words and are potentially insufficiently reported due to journal word count limitations. Using one rater for the STROBE checklist only may be a limitation of our review and some STROBE items may be judged subjectively to a varying degree. Of note, second ratings of five articles revealed only one single disagreement leading to a change. Evaluation is ongoing, results will be finalized prior to the EAACI Congress 2019.

TP0767 | Study of cases of hypersensitivity to low molecular weight heparins in an allergy unit

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Background: Cross-reactivity (CR) between heparins is frequent; therefore, identification of therapeutic alternatives is essential. Our objective was to analyze clinical and allergic characteristics of patients with hypersensitivity to Low Molecular Weight Heparins (LMWH) and to determine safe alternatives.

Method: We analyzed the patients reporting hypersensitivity reactions to LMWH referred to the Allergy Unit in our hospital during the period 2012-2018. We reviewed clinical data and the allergy study performed: patch tests (PT), skin prick tests (SPT) intradermal tests(IDT) and subcutaneous challenge test (SCT) to the culprit LMWH, other LMWH or Fondaparinux. Drug allergy was confirmed if cutaneous tests or subcutaneous provocation were positive.

Results: Seventy six patients consulted for suspected adverse reaction to LMWH 52 completed the scheduled study. LMWH allergy was confirmed in 28 (52.8%), 93% women, median age 63 years (range 32-83 ys). 89% patients had delayed reactions. 93% were local reactions (erythema eczematous plaques in injection site). 7% presented maculopapular exanthema. Approximately 2/3 of the patients began with the reactions between 1 to up 4 days from heparins treatment onset.

IDT were performed in 25 patients with 38 (28.3%) positive results of tested heparins. PT were positive for all LMWH in 1 of the five patients tested. We performed 45 SCT with the LMWH involved and /or alternatives in the 28 allergic patients. 21 of 45 SCT were positive.

Out of all the patients diagnosed of allergy to LMWH: 35.7% were diagnosed of allergy to a single heparin, 21.4% to two heparins and 49% to three or more. In our series, three women had reactions during pregnancy, all of them had hypersensitivity to more than one LMWH.

We found CR in 17 patients (60.7%) without any clear pattern of association between heparins. Thirteen patients who did not tolerate other LMWH were challenged with Fondaparinux, which was tolerated in all of them.

Conclusion: Enoxaparin was the most commonly involved LMWH (both by suggesting history and allergy study) due to its frequent use in our area. High CR between heparins was observed.

LMWHs different,from those involved, in several patients were tolerated. Fondaparinux was a safe option in our patients.

TP0770 | Infection risk assessment of epinephrine auto-injectors in vitro

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Background: In allergic emergencies, it is common practice to inject epinephrine through worn clothing. Infections even with highly pathogenic bacteria have sporadically been observed after use of epinephrine auto-injectors (EAI). A critical determinant to develop an infection is the adherence of sufficient bacteria to needles. Since data on adhesion behavior is lacking we quantified reference bacterial species on EAI needles.

Method: *Staphylococcus aureus* BA976, *Escherichia coli* ATCC25922, *Staphylococcus epidermidis* 1585, *Bacillus subtilis* ATCC23857 spores were grown, harvested and suspended in concentrations of 10^3, 10^6, and 10^8 CFU/mL using standard microbiologically techniques. Sterile steel needles were exposed for 3, 5, 10, and 60 s. Adherent bacteria were removed and plated for quantification. To determine the influence of storage on adherent cell replication, needles were placed in a sterile dry tube for 5, 15, 60 min, and 24 h.

Results: After 60 s, suspensions of 10^3 CFU/mL showed no adherence to needles. Suspensions of 10^6 and 10^8 CFU/mL showed adherence of 13-40 cells and 1453-9400 cells respectively. After 5 min storage low numbers of adherent bacteria could be recovered from the needle (430 CFU/mL [*B. subtilis*] and 3800 CFU/mL [*S. aureus*]). Storage of needles over time resulted in a decline of viable adherent bacteria for *S. aureus* and *E. coli*. The amount of adherent *B. subtilis* remained stable.

Conclusion: Extrapolating the results to the conditions of human skin, carrying roughly 10^2 CFU/cm^2, adherence of significant numbers of bacteria and their replication above the infective threshold of 100 bacteria per needle, is most unlikely. Therefore, the use of EAIs is microbiologically safe.

TP0771 | Epinephrine auto-injector administration Results in consistent delivery across subjects with different skin-to-muscle distances

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Background: Intramuscular (IM) injection of epinephrine administered via an epinephrine auto-injector (EAI) is the standard therapy for anaphylaxis. Though the needle length of an EAI (15.24 mm) has been suggested to reach thigh muscle in most people, such needle lengths may not penetrate beyond the subcutaneous layer of fat in those with a greater skin-to-muscle distance (STMD). This study was performed to analyze whether EAIs can provide systemic delivery of epinephrine across people with varying STMD.

Method: This open-label, single-dose, randomized, crossover study investigated the PK (eg, peak epinephrine plasma concentration [C_{peak}], time to C_{peak} [t_{peak}]) of epinephrine delivery via EAI vs IM syringe in subjects with varying STMD. Subjects (n = 35) were stratified into 3 sex-balanced groups on the basis of STMD: low (<15 mm), moderate (15-20 mm), or high (>20 mm), determined by ultrasound. Each subject received 3 injections at the mid anterolateral (AL) thigh on separate days in a randomized order: EAI (0.3 mg/0.3 mL), IM epinephrine via syringe (0.3 mg/0.3 mL), or saline (0.3 mL). Subjects with skin-to-bone distance (STBD) ≥ 20 mm at the distal AL thigh received a fourth injection (EAI, 0.3 mg/0.3 mL) at that site (subjects with STBD < 20 mm were excluded for safety reasons). In this assessment, model-independent PK parameters for epinephrine after EAI administration were compared across STMD groups. Correlations with anthropometric measurements (eg, BMI, STMD) were assessed (Pearson r and Kendall tau).

Results: C_{peak} was similar across STMD groups; t_{peak} was longer in subjects with high STMD compared with low or moderate STMD for EAI injections at the mid AL thigh, and early exposures within 30 min (based on partial AUCs) suggested a slight lag with respect to increased STMD. These between-group estimates were highly variable. Partial AUCs indicated more rapid delivery of epinephrine within the first 30 min for EAI vs IM syringe across all STMD groups. Injection via EAI at an alternative site with lower STMD (distal AL thigh) did not improve C_{peak} or t_{peak} vs mid AL thigh. There were no meaningful correlation coefficients (ie, r or tau > 0.5) between PK parameters and any anthropometric measurement. Treatments were well tolerated; 24 subjects experienced ≥ 1 AE, with the most common being palpitations and headaches.

Conclusion: Systemic delivery of epinephrine via EAI was consistent across subjects with varying STMD even if the needle length was too short to reach the muscle layer.

TP0772 | Perceived immune functioning before and after switching to raw milk consumption: A retrospective survey among us adults

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Background: Although there are still some microbial safety concerns with the consumption of raw milk (RM) and RM products, its use is increasingly popular, and positive health effects are reported by consumers. The purpose of this study was to examine consumer health effects of switching to RM products in a US population.

Method: Raw milk consumers were invited to complete an online survey. They were recruited at various US farms where they ought RM products. Data were collected on demographics, including the presence of chronic diseases. Subjects assessed their past health status (before switching to RM) and current health status (at least 2 months after switching to RM). The assessments included perceived immune functioning and health, which were scored on scales ranging from 0 (very bad) to 10 (very good), eleven gastrointestinal bowel complaints (e.g., abdominal pain and diarrhoea), and ten skin complaints (e.g., itching) were rated on a scale ranging from "all of the time" to "none of the time". Mood, including fatigue, tension-anxiety, depression/dejection, anger/hostility, and active/vigour, was rated on single item 5-point Likert scales ranging from "not at all" to extremely".

Results: N = 327 subjects completed the survey. They reported significant improvements in perceived immune functioning, mood, and health ($P < 0.05$) after switching to consuming RM, accompanied by a significant reduction ($P < 0.05$) in the presence and severity of gastrointestinal bowel symptoms and skin problems. The effects were seen across all subjects, but were significantly more pronounced in women, and among those who reported depressed immune functioning and/or chronic diseases before switching to RM.

Conclusion: Positive health improvements were reported by subjects after switching to RM products. The effects were most pronounced in women and immune depressed subjects with or without a chronic disease.

TP0773 | A case of eosinophilic hyperplastic lymphogranuloma on arm and eye orbit

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Case report:

Background: Eosinophilic hyperplastic lymphogranuloma (EHLG) is a rare form of chronic inflammatory disorder of unknown etiology. EHLG is a benign disease and seen mostly in young Asian men. EHLG is known to be associated with allergic diseases such as bronchial asthma and Candida sensitization, which suggests some immunological mechanisms may be related to the development of this disease. The recurrent rate is very high, up to 60%-80%.

Case: An 8-year-old boy. He first presented with a pruritic subcutaneous nodule on his left upper arm at 5 years of age. He was referred to our hospital at 8 years of age, because of the enlargement of the mass, axillary lymphadenopathy, eosinophilia (12 455/μl), and an elevated total IgE level (8382 IU/mL). Based on MRI findings and biopsy results, we diagnosed EHLG. After surgical excision and corticosteroid administration, eosinophilia and the total IgE level were improved to normal levels. However, while tapering of corticosteroid, number of peripheral blood eosinophils increased, and left eyelid swollen. MRI findings showed new EHLG lesion on lateral rectus muscle. We increased corticosteroid dose and started cyclosporine. Visual function was not disturbed.

Conclusion: This patient presented the first lesion on his arm. It was rare because that most EHLG occurred in the head and neck region. Surgical excision and corticosteroid administration were partially effective, and another lesion occurred during corticosteroid tapering. It shows the difficulty of EHLG management.

TP0774 | The co-existence and diagnosis of allergic & gastrointestinal symptoms in the adults with food allergy

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Background: It can be hard to distinguish between food allergy and gastrointestinal (GI) symptoms either alone or in conjunction with allergy. In food allergy clinic, it is important to evaluate both to offer a holistic approach to patients' symptoms. Hydrogen breath testing (HBT) may be a useful tool in helping diagnose symptoms due to disaccharide malabsorption which can be treated by dietary modification. We present two cases of patients with food allergy where HBT was useful, in the context of our new HBT service.

Method: Case 1 is a woman aged 55 who developed facial and upper airway swelling soon after eating a bean wrap. She had positive IgE tests to several legumes (lentil 1.02 IU/mL, chick pea 4.56 IU/mL, red kidney bean 1.40 IU/mL) and was diagnosed with a legume allergy. Despite avoidance, she experienced GI pain and diarrhoea on a regular basis. Case 2 is a woman aged 34 who had abdominal pain and vomiting with avocado and abdominal pain with banana, raspberry, artichoke, mango and pineapple. Skin test prick test was positive to avocado (4 mm) alone with a IgE 0.39 Iu/mL. She was diagnosed with an avocado allergy. Her abdominal symptoms continued despite avoidance. She had a previous positive lactose HBT.

HBT procedure: The patients followed an exclusion diet for 24 hrs, and fasted for 12 hrs before the test. Prior to the test, they provided an initial breath sample by blowing into the Gastrolyser™ machine. They then consumed a solution of lactose, glucose or fructose and gave subsequent breath samples for a period of up to 2 hours. A rise of 20 ppm above the baseline sample is considered diagnostic.

Results: Case 1 had a positive breath test to both lactose (increase by 78 ppb from baseline) and fructose (increase by 44 ppb from baseline). She was given dietary avoidance advice, which she observed. Her GI symptoms resolved.

Case 2 had a positive breath test to fructose (>100 ppm than the baseline). Her symptoms improved following dietary advice, though she did not have complete resolution.

From our food allergy clinic we have referred patients for an additional 89 HBT between July 2017 to December 2018 of which 17 (15%) were positive (9 fructose, 8 lactose).

Conclusion: Patients who present to food allergy clinic may benefit from HBT. Two cases presented here demonstrate the importance of rigorous tests for all symptoms. Targeted dietary advice following HBT can give patients significant benefit in addition to any current dietary restrictions for food allergy.

TP0775 | Significant hypereosinophilia accompanying an uncommon reason: Giardiasis

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Case report: Background: Giardia lamblia is one of the most common parasitic infection in the world. Despite two-thirds of cases with giardiasis are asymptomatic, clinical manifestations are variable and symptomatic patients present primarily with gastrointestinal problems such as diarrhea, steatorrhea, protein losing enteropathy, vomiting and weight loss. Rarely, hypersensitivity reactions such as rash, urticaria, and reactive arthritis may be seen. Hypereosinophilia is a rare comorbid condition. Here, we present a patient who was evaluated for epigastric pain and hypereosinophilia and got the final diagnosis of giardiasis.

Case report: A fourteen years old girl presented to our pediatric gastroenterology unit with complaints of epigastric pain and nausea for the last 3 days. She had no symptoms of vomiting, weight loss, diarrhea, constipation, fatty stool or melena. Due to her clinical reports, she admitted to another hospital with similar complaints 4 months ago and empirical proton pump inhibitor therapy was given for 15 days. Blood tests and endoscopy were planned in case of unresponsiveness.

At admission, epigastric tenderness and urticarial maculopapular rash were determined. Serial hemogram levels showed that absolute eosinophil counts were 3290, 4780 and 7550 cells/microL, respectively. The patient was also evaluated in our pediatric allergy unit for hypereosinophilia. Peripheral blood smear showed no atypical cells. Recurrent stool tests showed no parasites. Her echocardiographic evaluation was normal. Due to intractable epigastric pain and hypereosinophilia, upper endoscopy was performed. In duodenal tissue giardia trophozoites accompanying mucosal eosinophils (80-100 eosinophils per high-power field) were determined. Her clinical symptoms and peripheral hypereosinophilia resolved soon after metronidazole treatment administered for 2 weeks.

Conclusion: Hypereosinophilia is an extremely rare condition encountered in giardiasis and underlying mechanism(s) are still not understood. This case underlines the importance of evaluating absolute eosinophil counts in patients with systemic symptoms. Parasitic infections should be investigated insistently and giardiasis should also be taken into account in case of hypereosinophilia.

TP0776 | Chemiluminescence activity of neutrophil granulocytes and monocytes in blood in children with helicobacter pylori-associated erosive ulcer lesion of stomach and duodenum

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Background: The aim of the research is studying chemiluminescence activity of neutrophil granulocytes and monocytes in blood in children with *Helicobacter pylori* — associated erosive ulcer lesion of stomach and duodenum.

Method: Materials of the research were represented by neutrophil granulocytes and monocytes of blood, expressed from the blood of 46 subjects having *H. pylori*-associated erosive ulcer lesion of stomach and duodenum in the ages from 11 to 18 years and in 55 practically healthy subjects. Study for oxygen-dependent phagocytosis of monocytes and neutrophil granulocytes in blood was carried out by chemiluminescence method.

Results: There search for oxygen-dependent phagocytosis in a cohort of patients showed a considerable decrease of the time of reaching the peak and the growth of intensity and increased area under the curve of luminol-dependent spontaneous response as compared to control. In the process of neutrophil granulocytes induction, we observed the lowering of the time of reaching the peak and the growth of intensity as compared to control. Comparative analysis of the respiratory activity of the common fraction of neutrophil granulocytes and monocytes showed the increase of the intensity in the luminol-dependent spontaneous and zymosan-induced process in neutrophil granulocytes. The area under the curve is decreased as compared to the common fraction of blood monocytes. The study for lucigenin-dependent process showed avaricious increase in the activity of the common population of neutrophil granulocytes both in spontaneous response and zymosan-induced process in relation to blood monocytes. However, activation index is increased in neutrophils.

Conclusion: In terms of the comparative aspect, we revealed the decreased area under the curve of blood monocytes in relation to neutrophil granulocytes, which reasonably characterises the insufficiency of cytotoxic activity of monocytes in comparison with neutrophils.

TP0777 | Primary Sjogren's syndrome in serbian patients: Evaluation of health—Related quality of life and fatigue

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Background: The aim of the study was to evaluate health-related quality of life (HR-QoL) and fatigue in patients with primary Sjogren's syndrome (pSS).

Method: Forty-one consecutive patients with pSS according to AECG criteria, treated from October 2017 to April 2018, at the Clinic of Allergy and Immunology, Clinical Center of Serbia, were included in the study. HR-QoL was evaluated using SF-36 questionnaire and compared with the reference values for a healthy population. Fatigue was assessed using Fatigue Severity Scale (FSS). Demographic, clinical and immunological characteristics for all patients were collected.

Results: Most of the patients were women - 92.7%. The mean age was 56.2 ± 13.5 years. The most frequent clinical manifestations were ocular dryness (85.4%), oral dryness (82.9%), joint involvement (56.1%), constitutional symptoms (24.4%) and lymphadenopathy (9.8%). The patients with pSS showed lower scores in all SF-36 domains except for global health (GH) (P = 0.089), vitality (VT) (P = 0.159) and mental health (MH) (P = 0.8345) compared with healthy population. More than half of patients (53.6%) had pathological values of FSS score (FSS > 4.8). There was significant negative correlation between FSS score and HR-QoL, especially in mental composite score (MCS) (rho = -0.709, P < 0.001), physical composite score (PCS) (rho = -0.775, P < 0.001) and physical functioning (PF) (rho = -0.823, P < 0.001). There was no significant difference in SF-36 scores according to the presence or absence of sicca features (ocular dryness P = 0.119, oral dryness P = 0.282)). Patients with constitutional symptoms had lower scores for PCS (P = 0.0299), PF (P = 0.0233), social functioning (SF) (P = 0.0305), VT (P = 0.0296) and bodily pain (BP) (P = 0.00979), and those with joint manifestations had lower sores for PF (p0.0242), role physical (RP) (P = 0.0227), BP (P = 0.000675) and PCS (P = 0.0051).

Conclusion: Our data showed reduced HQ-QoL compared to the healthy population and a high prevalence of fatigue in patients with pSS. Constitutional symptoms, joint manifestations and fatigue severity have been related to the reduced HR-QoL. Appropriate therapeutic management of these manifestations may contribute to the improvement of the HR-QoL in patients with pSS.

TP0779 | The immune status questionnaire (ISQ): Further validation in a Dutch and international sample

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Background: There is a need for validated instruments to assess immune fitness in order to have a quick and accurate impression of immune status, without the need of invasive assessments. For this purpose the Immune Statius Questionnaire (ISQ) was developed. The aim of the current two studies was to further validate the ISQ in a Dutch and International sample.

Method: The Dutch Survey was held among N = 258 Dutch adults (Mean (SD) age = 22.9 (3.4)), and the International Survey was held among N = 374 subjects from various nationalities (Mean (SD) age = 24.8 (6.7)). In both surveys, past year immune status was assessed with the 7-item Immune Status Questionnaire (ISQ) and current perceived immune functioning was rated on a scale ranging from 0 (very poor) to 10 (excellent). In the Dutch survey, various factors that potentially impact immune fitness were assessed, including sleep duration, sleep quality, the use of alcohol, drugs and tobacco, daily activity level, body weight, hours of sports per week, and days of consuming healthy food or fast food. In the international survey, stress, anxiety, depression, anger/hostility, being active, and fatigue were assessed on 11-point scales ranging from 0 (absent) to 10 (extreme).

Results: In the Dutch survey, the mean (SD) ISQ score was 6.4 (2.5). ISQ scores correlated significantly with perceived immune functioning (r = -0.384, P = 0.0001), sleep quality (r = -0.212, P = 0.01) and body weight (r = -0.128, P = 0.039). No significant correlations were found between ISQ and the other assessed variables. In the International Survey, the mean (SD) ISQ score was 5.8 (3.2). ISQ scores correlated significantly with perceived immune functioning (r = -0.358, P = 0.0001), stress (r = 0.162, P = 0.002), anxiety (r = 0.133, P = 0.010), depression (r = 0.169, P = 0.001), and fatigue (r = 0.132, P = 0.010).

Conclusion: In both studies the ISQ scores were comparable and correlated well with current perceived immune functioning. The International Survey revealed that immune status as assessed with the ISQ correlates significantly with psychological health and mood. The Dutch Survey showed that ISQ scores correlated significantly with sleep quality and body weight. The lack of significant correlations with other known factors that may impact immune fitness (e.g., smoking and alcohol consumption) may be due to the relative young age of the sample and their overall good health status. Future studies in older populations with a more variable health status are needed.

TP0780 | The positive effects of having a holiday on immune fitness, psychological health, and mood

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Background: Contemporary society poses great psychological and physical demands on people, which may result in complaints such as stress, being overworked, and sleep disturbances. This exposome pressure will ultimately result in reduced immune fitness and illness. It is therefore essential to have regular free-time and/or holidays to reset the body and brain. The aim of the current study was to assess the impact of having a holiday on perceived immune functioning, psychological health, and mood.

Method: A survey was held among N = 281 adults who were on holiday in Fiji, and N = 93 subjects who went there to work. Past year immune status was assessed with the Immune Status Questionnaire (ISQ). Current perceived immune functioning was rated from 0 (very poor) to 10 (excellent). Using similar 11-point scales, stress, anxiety, depression, anger/hostility, and fatigue were assessed (0 = absent to 10 = extreme) for 2 occasions: (1) the current situation (being on Fiji), and (2) before going to Fiji (being at home).

Results: Correlational analysis comparing ISQ scores (before going to Fiji) and perceived immune functioning (while at Fiji) revealed a significant improvement in perceived immune functioning for those on holiday (r = -0.467, P = 0.000) and a nonsignificant improvement for those working (r = -0.196, P = 0.060).

Compared to being at home, subjects on holiday in Fiji reported significantly lower levels of stress, anxiety, depression, anger/hostility, and fatigue, and being significantly more active (P < 0.0001). For those working at Fiji, a significant reduction was only reported for stress, depression, anxiety, and anger-hostility. The magnitude of improvement reported for stress, depression, anxiety, and anger-hostility of both groups was comparable. For example, both groups reported a 60% reduction of stress while on Fiji. For those on holiday, the number of days spent at Fiji was significantly associated with a reduction in stress, anxiety, depression, and fatigue (P < 0.05). None of the correlations were significant for those who went to Fiji to work.

Conclusion: The data suggest that both having a holiday or working in Fiji significantly improves immune fitness, psychological health, and mood. The reported improvements were most pronounced for those who had a holiday, and the magnitude of improvement was significantly associated with the duration of being on Fiji.

TP0781 | Exposome pressure on immune fitness: A layman's perspective

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Background: Immune fitness is a complex concept which can be influenced by both internal factors (the genome) and external factors (the exposome). The current study explored the layman's perspective on how exposome pressure (e.g., lifestyle and diet) influences immune fitness.

Method: N = 297 subjects, aged 18 years and older, completed an online survey on immune fitness. The impact on immune fitness of 23 exposures were rated on a scale with the anchors 'very negative' (-2), 'negative' (-1), 'neutral' (0), 'positive' (1), and 'very positive' (2). The exposures covered (a) dietary intake (fruit, vegetables, fibers, salt, sugar, candy, pre- and probiotic supplements), (b) lifestyle factors (smoking, alcohol, sports activities, having a white-color job, a normal body weight, shiftwork, irregular sleep, being outdoors regularly, stress, and personal hygiene), and (c) health-related factors (e.g., having had childhood diseases, childhood vaccinations, being born via a Cesarean section, and the use of painkillers, anti-inflammatory drugs, or antibiotics).

Results: The most positive impact on immune fitness (P < 0.0001) was reported for being engaged in sports activities (90.1% positive; M= +1.31), being outdoors regularly (90.5% positive; M = +1.13), eating vegetables (86.0% positive; M = +1.12), and attaining a normal body weight (81.4% positive; M = +1.02). The most negative impact on immune fitness (P < 0.0001) was reported for stress (92.1% negative; M = -1.28), smoking (80.1% negative; M = -1.25), alcohol (80.1% negative; M = -1.07), and irregular sleep (82.2% negative; M = -1.07). Factors with the reported most neutral impact on immune fitness included having had childhood diseases (73.6% neutral; M = +0.09, P = 0.099) and the use of painkillers (82.6% neutral; M = -0.09, P = 0.055).

Conclusion: Being engaged in sports and stress were identified as most positive and negative factors impacting immune fitness, respectively. The layman's perspective was not always in agreement with the scientific evidence. Given this, it is useful to educate the general public in order to increase their knowledge on how various factors impact immune fitness.

TP0782 | Acute alcohol effects on cytokine concentrations in healthy young adults

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Background: A common example of exposome pressure on immune fitness is the consumption of alcohol. In a previous study we

demonstrated that the morning following an evening of heavy alcohol consumption (i.e., during alcohol hangover) significant increases of cytokine concentrations of IL-6 and IL-10 were observed. The aim of this study was to examine salivary cytokine concentrations over time in the first 7 hours directly after the consumption of alcohol.

Method: N = 17 healthy young adults participated in an experimental study, comprising an alcohol test day and alcohol-free control day. A saliva sample was collected at baseline, i.e. before beverage consumption (alcohol or placebo) (timepoint 1). Subsequently, they consumed alcohol on the alcohol test day (to reach a BAC level of 0.08%) or received a placebo drink on the control day. Saliva was collected hourly for 7 hours, using the passive drool method (timepoint 2 to timepoint 8). Saliva concentrations of IL1β, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, GM-CSF, IFN-γ and TNF-α were assessed for each timepoint. Only those cytokines that could be reliably determined on multiple timepoints (<25% under the lower limit of detection) were used for statistical analysis. Outliers (>3SD difference from group average) were removed from the dataset. To correct for day-to-day variance in cytokine concentrations, baseline-corrected data were used for the analysis: the difference score (alcohol minus control) on T1 (baseline) was subtracted from all subsequent alcohol measurements (T2 to T8). GLM for repeated measures was used to compare cytokine concentrations on the alcohol and control day across the timepoints. Differences were considered significant when $P < 0.05$.

Results: For N = 15 participants the salivary cytokine concentrations of IL-1β, IL-8, TNF- α could be reliably determined. Relative to the control day, significantly increased salivary cytokine concentrations were found on the alcohol day for IL-1β on time points T2 ($P = 0.038$), T3 ($P = 0.048$), and T8 ($P = 0.0001$). No significant differences were found for IL-8 and TNF-α.

Conclusion: The current findings confirm that acute alcohol consumption has a direct increasing effect on cytokine concentrations in healthy young adults. However, the observed effects are of a much smaller magnitude as those seen when alcohol is consumed in the evening and cytokine concentrations are assessed the following morning, approximately 9 hours after stopping drinking.

SUNDAY, 2 JUNE 2019
TPS 10
BIOLOGICALS AND THERAPEUTIC APPROACHES IN ASTHMA

TP0783 | Real life data on treatment response to mepolizumab in patients with severe eosinophilic asthma

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Background: Mepolizumab is a humanized monoclonal antibody which targets interleukin-5 (IL-5) and is an add-on biological therapy of severe eosinophilic asthma. We present real life clinical data of our patients who treated with Mepolizumab over 6 months.
Method: All patients receiving mepolizumab for the treatment of asthma according to the EMA indications during the first 6 months after drug release in Greece were prospectively evaluated. We record demographic data, quality of life based on the St. George questionnaire (SGRQ) and the treatment response assessed by FEV_1%pred, asthma control questionnaire (ACT) and exacerbations. All subjects provided informed consent for publication of their data.
Results: A total of 11 patients (7/11 females, 45.5 years, range: 30-57 years) who had history of asthma with mean disease duration 12.9 years (range 1-40) received mepolizumab. The mean absolute eosinophil count of patients was 807 cells/μL (range: 158-2330) prior to mepolizumab treatment. Four patients discontinued treatment; 2 of them due to lack of response, one because of myalgia after the first administration and the remaining one for personal reasons. Referring to the 2 non-responders; the first was a 49 year old male who had received omalizumab in the past with partial response and experienced a severe exacerbation with 27.9% FEV_1 decline after the first administration. The second patient was a 37 year old female who had an absolute eosinophil count of 2330 cells/μL prior to initiation and despite the dramatic decrease of eosinophil count (130 cells/μL 25 days after the first dose) no clinical response was observed during the 6 months. The remaining 7/11 patients who continued treatment at 6 months had 18.1% mean increase of FEV_1 (range: 0-37.7%); 57.6% mean increase of ACT (range: 0-200%); improvement in SGRQ by 49.5% (range: 5.1-97.7%). Among the responders' subgroup during the 6 months of mepolizumab only 2 patients experienced exacerbations (one each) compared with the average 2.29 exacerbations/year, (range: 0-6) that 6 out of 7 patients had during the previous year .
Conclusion: Use of mepolizumab in clinical practice confirms data from clinical trials when administered to appropriately selected patients.

TP0784 | Mepolizumab for the treatment of severe eosinophilic asthma: A real-life study of 27 patients

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Background: Mepolizumab is a humanized monoclonal antibody raised against interleukin-5. In clinical trials, its efficacy was shown by reduction of asthma exacerbation rate and improvement FEV_1 in severe eosinophilic asthma patients. However, patients in real-life are more complex compared to those in clinical trials. On the other hand real-life studies investigate effectiveness often providing additional information, which cannot be retrieved from clinical trials.
Method: A retrospective review of patients with severe eosinophilic asthma treated with mepolizumab (100 mg administered subcutaneously every 4th week) was performed. Demographic data, FEV_1 percent predicted, FEF_{25-75} percent predicted, peak expiratory flow (PEF), eosinophilic blood count, number of disease exacerbations (defined as need to use or increase oral corticosteroids for more than 3 days or a hospitalization), rating of asthma control test and safety data were collected. In each patient we compared data relative to 12 months before the inception of treatment with mepolizumab with those collected after patients started mepolizumab (range 2 to 25 months, median = 11).
Results: 27 patients (19 female, mean age 53.4 ± 13.7 years old) were reviewed. The mean value for each outcome before and after mepolizumab treatment were the following: FEV1%, from 73.3% to 73.5%; $FEF_{25-75\%}$, from 48.5% to 50.1%; PEF, from 360 L/m to 366 L/m; mean eosinophilic blood count, from 550.8 to 91.8; number of disease exacerbations, from 46 to 19; rating of asthma control test, from 12.83 to 18.38. No local adverse reactions were reported. Mild systemic reactions were reported in 3 patients who complained headache, occasionally.
Conclusion: In real-life, patients with severe eosinophilic asthma achieved a measurable improvement in asthma outcomes by reduction of exacerbations, reduction of eosinophilic blood count and improvement of the quality of life. The clinical outcomes were better in patients with higher eosinophilic blood counts before the inception of mepolizumab treatment.

TP0785 | Evaluation of patients with severe asthma with 6 months of treatment with mepolizumab - The experience of the pulmonology services of 2 tertiary referral hospitals

Pereira IS[1]; Fernandes AL[2]; Silva MC[1]; Rodrigues D[2]; Vaz AP[2]; Neves I[2]; Correia S[2]; Franco I[1]; Ladeira I[1]; Pascoal I[1]; Carvalho A[1]; Ferreira J[2]; Lima R[1]

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Background: Mepolizumab is a monoclonal antibody indicated for the treatment of severe asthma that inhibits the bioactivity of IL-5 by blocking its binding to eosinophils, reducing their survival and function.

Method: Retrospective analysis of patients from the outpatient Pneumology-Asthma clinic of 2 tertiary referral hospitals with severe eosinophilic asthma with at least 6 months of treatment with Mepolizumab. The prednisolone dosage, corticosteroid cycles, FEV1 (Forced expired volume in the first second), peripheral eosinophils and score in ACT (Asthma Control Test) were compared at the beginning and after 6 months of treatment by the Wilcoxon test trough SPSS software. The objective of the study was to evaluate the clinical response to Mepolizumab in severe eosinophilic asthma after 6 months of treatment.

Results: To date, 20 patients with severe asthma started treatment with Mepolizumab, with 75% (n = 15) women, a mean age of 57.35 (+-10.56) years and a mean BMI of 30.58 (+-5.27) Kg/m2. Four patients (20%) had been previously treated with Omalizumab. One patient referred headache associated with Mepolizumab and another had an injection site reaction, but no drug discontinuation was required. In 10% (n = 2) of patients, Mepolizumab was discontinued because of a lack of clinical response.

In patients being treated with Mepolizumab for more than 6 months (n = 15), the prednisolone dosage, number of corticosteroid cycles, FEV1, peripheral eosinophils and score in ACT were evaluated before and after therapy. The results are presented in Table 1.

Conclusion: A 6-month treatment with Mepolizumab showed a statistically significant decrease in prednisolone dose, number of oral cortisone cycles and peripheral blood eosinophil count. A statistically significant clinical and functional improvement (assessed by ACT and FEV1 respectively) was also observed. No significant side effects were observed. Our real life data corroborate those previously presented by clinical trials.

TP0786 | Mepolizumab: Monocentric one-year experience

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Background: Purpose of our study is to describe our use of Mepolizumab to treat patients (pts) with a severe refractory asthma to confirm the expectations that using monoclonal antibodies in the management of severe asthma is a valid support in most cases.

Method: At our institution, we treated with Mepolizumab a group of 7 (5M/2F) pts with history of severe refractory asthma. Mepolizumab was started for pts who were in therapy with high-dose inhaled steroids and long-acting beta-2-agonists (ICS/LABA), with 2 or more flare/year requiring either oral steroid and/or hospitalization, and with eosinophilic count at baseline > 150 cells/m^3. Other clinical conditions worsening asthma (e.g. rhinosinusitis, cigarette smoke practice, overweight, gastroesophageal reflux and avoidance of allergenic exposure) were appropriately treated before initiating therapy. All pts were assessed for anti Ig-E therapy and did not meet treatment criteria.

Data were summarized as mean and standard deviation for normally distributed variables and as median with interquartile range (IQR) for non-normally distributed ones. Our observations should be considered purely descriptive as the sample size did not allow statistical comparisons.

Results: Mean age of our pts at baseline was 64.7 ± 10.9 years, with an average history of disease of 17.3 ± 12.8 years. Pts were followed for more than 1 year, with monthly medical visit, including clinical and spirometry evaluation. Correct use of inhalers devices was consolidated at each visit to optimize therapy adherence. All pts showed significant clinical improvement between 1 and 4 months after starting the therapy. None of the pts had to discontinue therapy and none of them experienced any side effect.

During follow-up, Asthma Control Test (ACT) questionnaire results improved from 14 ± 2 to 24 ± 2; median FEV1 values increased from 2080 mL (IQR 1725-2480) to 2680 mL (IQR 2092.5-2697.5), median FEV1% increased from 79% (IQR 63%-84%) 87% (IQR 84%-95%); median eosinophils count decreased from 695 cells/m^3 (IQR

	Baseline (Mean ± SD)	6 months of Mepolizumab (Mean ± SD)	*Z* value	*P* value
Prednisolozne dosage (mg)	22.44 ± 15.25	7.00 ± 7.19	−2.375	0.018
Corticosteroid cycles	2.86 ± 1.61	1.33 ± 1.23	−2.669	0.008
FEV1 (%)	74.99 ± 26.86	81.69 ± 14.46	−2.062	0.039
Eosinophils	902.67 ± 632.37	75.00 ± 61.72	−3.065	0.002
ACT	9.20 ± 2.66	19.36 ± 3.11	−2.812	0.005

375-1097] to 60 cells/m^3 [IQR 45-142.5]. Symptoms of rhino-sinusal involvement disappeared at follow-up for all pts who described them at baseline.

Conclusion: In our experience, the use of Mepolizumab as an add-on therapy according to current guidelines is an effective and safe approach to improve pts's quality of life. Longer-term, larger scale, real-life observations and cost-benefit assessments are needed to confirm our current experience.

TP0787 | Treatment of severe asthma with mepolizumab: The influence of obesity

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Background: Severe asthma and obesity have a considerable impact on public health. Mepolizumab, an anti-IL5 monoclonal antibody, has demonstrated to improve symptoms, reduce exacerbations and utilization of oral corticosteroids in severe eosinophilic asthma. Detailed characterization of asthma phenotypes is essential for identification of responder populations. The aim of this study was to assess the impact of mepolizumab treatment in obese asthmatic patients.

Method: Retrospective multicentric study including severe eosinophilic asthmatic patients treated with mepolizumab and followed over a 6 months period. The study population was divided into two groups (obese and non-obese) for statistical analysis (descriptive and comparative analysis using SPSS software).

Results: We included 15 patients (10 obese/5 non-obese), mainly female (11-73.3%) with a mean age of 55.4 ± 10.5 years. Descriptive and comparative analysis before mepolizumab revealed no differences between the groups (obese/non-obese), except on eosinophils (604.0 ± 368.9/1500.3 ± 651.5 cels/μl; $P = 0.012$).

After 6 months of therapy, the comparative analysis demonstrated that the obese group had a lower dosage of corticosteroids (17.5 + -3.5/ 4.0 ± 4.4 mg; $P = 0.036$).

The analysis of each group after 6 months of treatment showed that obese patients had a statistically significant improvement in the dosage of corticosteroids (22.4 ± 17.1/4.0 ± 4.4; $P = 0.027$), number of corticosteroids cycles (2.7 ± 1.7/1.3 ± 1.1; $P = 0.046$), eosinophils (604.0 ± 368.9/60.0 ± 41.7; $P = 0.012$) and ACT (9.1 ± 2.9; 19.1 ± 3.6; $P = 0.012$); while the non-obese group had a statistically significant reduction in the need of corticosteroids cycles (3.3 ± 1.5/1.4 ± 1.5; $P = 0.042$).

Conclusion: There are a few studies in the literature that evaluate the impact of obesity in the mepolizumab treatment of severe eosinophilic asthma. Despite being a small sample, the obese group demonstrated significant improvement in symptoms and dosage of corticosteroids when compared with the non-obese group. So, more of studies are needed to explore the obese-asthmatic patients treated with mepolizumab.

TP0788 | Personalized approach to omalizumab asthma treatment - the phenotype concept. A single reference center experience

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Background: Although the clinical efficacy of omalizumab in asthma has a history of multiple studies, there is still a lack of prospective real-life clinical data with putting a stress on clinical phenotyping.

Method: To explore the complex effect of the treatment in different time-points with sub-grouping the cohort of patients by clinical features-risk factors (smoking status, BMI, low-fixed FEV1, the level of blood eosinophils). The analyze included retrospective baseline description and the prospective period.

Results: 38 patients, who reached at least the 16th week of treatment (from 46 currently under observation) with uncontrolled atopic severe asthma were included (m = 11, f = 27), fulfilling the criteria's of the diagnosis.

The treatment assessment included ACT (reaching more than 20 points), FEV1(%, L), exacerbation rate change for those, who reached 12 months, rhinomanometry parameters for those with allergic rhinitis and nasal polyposis. We compared the treatment response in groups (obese (n = 21) and non-obese (n = 17), smoking (n = 10) and no-smoking (n = 28), baseline FEV 1 lower (n = 20) or upper(18) 80%, high (n = 18) and low (n = 20) level of blood eosinophils was measures before treatment for biomarker-stratification)

Results: No difference in the complex assessment of the treatment efficacy was observed in the connection with the BMI index and blood eosinophils levels, the significant difference (ACT) ($P < 0.05$) was observed in the results of the groups with different smoking status and low-fixed obstruction, the percentage of the responder (ACT ≥ 20) at the time-point of 16 weeks was only 50% responders in the smoking group (in comparison with non-smoking 70%) and 55% responded with baseline FEV1 < 80% (in comparison with 70% in the group with baseline FEV1 ≥ 80%)

Conclusion: The pilot results demonstrate that some of the bronchial asthma clinical phenotypes can have later response to the IgE treatment, and preliminary stopping can cause the dismissing of later- responders, who have chances to benefit from the treatment. The number of observations must be expanded in order to have an attempt of creating a mathematical model of the phenotype prognosis of the treatment response. The assessment of treatment

response has to be complex in asthma patients and can be individualized by clinical phenotype-approach.

TP0789 | Efficacy of omalizumab therapy after 5 years of follow-up

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Background: Monoclonal antibodies directed against IgE and interleukins have changed the paradigm of severe persistent asthma. Omalizumab is the drug that has been the longest in the market; however, few studies have evaluated its efficacy for a long period of follow-up. Our aim is to evaluate the sustained efficacy of omalizumab after five years of follow-up.

Method: Observational and retrospective study of the clinical records of adult patients followed in a severe asthma medical appointment under omalizumab. Analysis of asthma control with Asthma Control Test (ACT), exacerbations rate, systemic corticosteroids use and lung function (FEV1 and PEF) after five years of follow and comparison with their status after 1 year of follow-up and previous status before omalizumab.

Results: The total number of patients analyzed was 11, being 9 female (81.8%) with an average age of 54 years old. The comparison of the results at 5 years of treatment with omalizumab with the pretreatment period showed: a significant ($P < 0.05$) improvement in the mean ACT average score of 44.6% (13 to 18.8); a significant ($P < 0.05$) improvement in the average FEV1 of 24.5% (58.7 to 73.1); a significant ($P < 0.05$) improvement in the average PEF of 35.7% (235 mL to 319 mL). The results at 5 years of follow-up were similar with those at 1 year of follow-up - mean ACT score: 20.7 (vs 18.8 at year 5); average FEV1: 75.1 (vs 73.1 at year 5); average PEF: 345 mL (vs 319 mL at year 5). Furthermore, before omalizumab 10 patients (90.9%) used systemic corticosteroids at least once per month and at 5 years of follow-up 7 patients (63.6%) had stopped using them (the same number as after 1 year of follow-up). Finally, before omalizumab all patients (n = 11; 100%) had exacerbations on a monthly basis and at 5 years of follow-up 7 patients (63.6%) no longer exacerbated, which is higher than the number of patients (n = 5) without exacerbations after 1 year of follow-up.

Conclusion: The results show that omalizumab has improved significantly all the parameters analyzed and that the improvement is sustained throughout time, which proves its effectiveness and reliability over a long term and continued benefits in reducing symptoms and exacerbations.

TP0790 | Can peripheral eosinophilia in aspirin-induced airway disease (AERD) increasing tendency after aspirin desensitization therapy?

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Background: There are many clinical studies showing that ASA (acetylsalicylic acid) use in ASA-exacerbated airway disease (AERD) reduces the symptoms of ASA use after desensitization. Eosinophil levels were shown to increase in the early period of treatment and desensitization. We observed that in some of AERD patients, eosinophil levels were increased in some patients and decreased in some after ASA desensitization treatment. In our study, we aimed to investigate the factors that reversed the peripheral eosinophil increase after ASA desensitization in AERD patients.

Method: The patients who underwent ASA desensitization for AERD were evaluated retrospectively. In addition to ASA 600 mg/day and standard asthma treatment, 4 patients were receiving anti-IgE (omalizumab) treatment. Age, gender, duration of asthma, number of polypectomy, duration of aspirin treatment, interval between polypectomy-desensitization time, improvement in symptoms after treatment, baseline and post-treatment eosinophil levels, total IgE levels and spirometric measurements were recorded.

Results: 13 patients with a mean age of 41.5 ± 11.6 years were enrolled in the study. The mean time interval between polypectomy and ASA desensitization was 19.6 ± 2 months. In 1 patient, ASA treatment was discontinued after a decrease in hearing and development of tinnitus in the first month of treatment. No serious side effects were seen in other patients. Mean FEV1 levels, decrease in eosinophil levels, and increase in total IgE levels were not statistically significant. The duration of asthma and the interval between polypectomy and ASA desensitization were significantly lower in the decreased eosinophil level group when compared with the increased eosinophil level group. The number of patients receiving Omalizumab was similar in both groups, but eosinophils were found to be more likely to fall in patients receiving Omalizumab ($P = 0.93$).

Conclusion: Our study was the first to show that eosinophil levels decrease after ASA desensitization treatment. The factors affecting this condition are the duration of asthma and the interval between polypectomy and aspirin desensitization. If ASA desensitization therapy is applied before the asthma duration prolonged and within the first month after polypectomy; the increase in eosinophils can be reversed.

	pre-desensitization	post-desensitization	*P*-value
FEV1(lt)	3.2 ± 0.9	3 ± 0.55	0.42
Eosinophil (/μL)	507 ± 286	463 ± 388	0.56
Eosinophil (%)	6.9 ± 4.2	6 ± 5.1	0.33
Total IgE	389 ± 323	563 ± 431	0.22

TP0791 | Omalizumab in real life: A retrospective study investigating clinical and airway inflammatory outcomes

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Background: Omalizumab arose as a therapeutic option in patients suffering from moderate to severe refractory allergic asthma. It acts as a humanized monoclonal antibody that neutralizes circulating IgE antibodies. Randomized clinical trials and real life clinical studies have already confirmed the benefits, cost-effectiveness and applicability of this medication.

Method: Our study reports on the clinical outcomes and airway inflammation in 136 severe allergic asthmatics who were initiated with omalizumab between 2007 and 2017 at our Asthma Clinic. Despite chronic treatment with high dose inhaled corticosteroids and inhaled long-acting β_2 agonist bronchodilators, asthma was still poorly controlled, with an ACQ averaging 3.04 and an exacerbation rate of 1/y at baseline. Median blood eosinophil count, total serum IgE and FeNO were high, reaching 228/µl, 248 Ku/L and 24 ppb respectively, indicating a current T2 pattern. Moreover, sputum eosinophils and neutrophils were also found to be high at baseline, with a median of 3% and 59% respectively.

Results: Seventy eight % (107/136) of the patients were judged to have benefited from omalizumab therapy after 4 months of treatment and were admitted to prolonged treatment. During follow-up, we observed an improvement in asthma control, quality of life and baseline airway calibre. There was also a sustained reduction in exacerbation rate over the years, by more than 25%. As for T2 biomarkers, FeNO significantly decreased and, in a subgroup of patients who had repeated sputum inductions, there was also significant reduction in sputum eosinophils but no change in blood eosinophil count.

Conclusion: We conclude that omalizumab shows effectiveness in severe allergic asthma in a real life setting, by reducing exacerbation rate, improving patient perspective outcomes and airway calibre, together with reducing T2 airway inflammation.

TP0792 | Omalizumab in the treatment of eosinophilic granulomatosis with polyangiitis (EGPA): Single-center experience in 18 cases

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Background: Data are limited regarding the effectiveness of omalizumab in patients with eosinophilic granulomatosis with polyangiitis (EGPA). Our aim was to evaluate the clinical and functional effectiveness of omalizumab in patients with EGPA in long-term follow-up.

Method: This study was a retrospective chart review of patients with EGPA who were treated with omalizumab injections between May 2012 and April 2018. Once treatment with omalizumab was started, data were collected at various time points: baseline, the 16th week, 1st year, and annually until the last evaluation.

Results: Eighteen patients (16F/2M) with a mean age of 48.61 ± 11.94 years were included. Data were available for all patients for the first year, 12 patients for the second year, 10 patients for the third year, 8 patients for the fourth year and 5 patients for the fifth year. All patients were on mean dosage of 15.77 ± 7.6 mg/day oral corticosteroid (OCS) as daily bases for mean 8.61 ± 4 years besides high-dose inhaler corticosteroid/long-acting beta agonist. Antineutrophil cytoplasmic antibodies (ANCA) were positive in 2 patients, and 8 patients were diagnosed as having vasculitis by skin biopsy, one patient had polyneuropathy, and one patient had cardiac involvement.

By considering the individual responses of patients and the level of improvement at the last evaluation, 10 (55.6%) patients responded completely, 1 responded partially, and 7 (38.9%) had no improvement. Omalizumab worked as a steroid-sparing agent in all patients and the daily OCS dose was reduced with a mean dosage of 6.28 mg/day at the end of the first year. The mean OCS reduction time for the whole group was 4 months. A reduction in asthma exacerbations/hospitalizations, improvement in forced expiratory volume in 1 second, and no decrease in the eosinophil count during treatment with omalizumab were also observed.

Conclusion: Omalizumab improved asthma control in some patients with EGPA with uncontrolled asthma by reducing asthma exacerbations and oral steroid requirement. However, more data are needed before recommending widespread use of omalizumab in patients with EGPA.

TP0793 | Beta2 agonists and doping: The potential to improve physical performance in athletes

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Background: During the last few years there has been an increasing debate on whether the ß2 Agonists have the potential to improve physical performance in athletes. The evidence regarding this topic remains controversial, with some studies supporting this claim and others supporting otherwise. Therefore, the aim of this systematic review is to assess the effects of inhaled or systemic ß2 Agonists on physical performance in healthy, non-asthmatic athletes.

Method: PubMed, Scopus, Science Direct, ISI Web of Science and Cochrane Library were systematically searched to identify studies

assessing the effects of ß2-Agonists on the physical performance in healthy individuals. The electronic databases were searched from inception through December 2018. We excluded studies performed in animals, in vitro studies, studies performed in children or adolescents and studies performed in non-healthy populations. The outcomes measures of interest included maximal oxygen uptake (VO_{2max}), endurance time to exhaustion, duration time of a time trial, Wingate test, maximal voluntary isometric contraction of muscles and agility.

Results: The initial search strategy yielded 115 citations, of which 88 studies were eligible for full test evaluation. Of these, 62 were included in the systematic review. We identified 24 studies which assessed the effects of β2-Agonists on VO_{2max}. Only one study reported a significant increase in this parameter after administration of a ß2-Agonist. Regarding endurance time to exhaustion, 9 studies showed none significative results, while 2 studies showed a reduction in the endurance time to exhaustion after inhalation of salbutamol. Of the 21 studies that assessed the effect of ß2-Agonists on the Wingate Test, the majority did not report significant differences.

Conclusion: Overall, this systematic review shows that ß2-Agonists do not improve physical performance, even at concentrations above those allowed by World Anti-Doping Agency (WADA).

TP0795 | Asthma-related outcomes in a real-world study of MP-AzeFlu to treat allergic rhinitis

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Background: Asthma is a common comorbidity that affects 20-30% of individuals with allergic rhinitis (AR). Results of observational studies indicate that treating AR lowers the risk of asthma-related hospitalizations and emergency visits. Studies also show that the total annual medical costs and prescribing frequency of asthma-related medications are higher for patients with AR and asthma. MP-AzeFlu treatment has been proven to be effective for the relief of AR symptoms. We evaluated use of MP-AzeFlu in routine clinical practice to assess the effect of treatment on asthma symptoms and the frequency of asthma reliever medication usage in patients with AR and comorbid asthma.

Method: This is the German part of a multinational, multicenter, prospective, noninterventional study that was designed to assess, in response to therapy, asthma symptoms and the frequency of asthma reliever medication usage in routine clinical practice by a Visual Analogue Scale (VAS). Patients with moderate-to-severe AR (AR symptoms VAS ≥ 50 mm) presenting with acute AR symptoms on inclusion day, for whom MP-AzeFlu has been prescribed for the first time and according to the summary of product characteristics and patient information leaflet, were included. Patients with comorbid asthma recorded how bothersome their AR and asthma symptoms were on the printed VAS provided in the patient card at the appropriate range (not at all bothersome = 0; extremely bothersome = 100 mm). Patients also compared the frequency of asthma reliever medication usage before and after the treatment period of 14 days.

Results: Of 450 total patients with AR, 105 (23%) had comorbid asthma and reported using asthma reliever medicine an average of six times in the week prior to starting treatment. 71% of participants with AR and asthma responded to therapy (achievement of AR-VAS score < 50 mm at least once during the treatment period), compared with 81% of total participants who also responded to therapy. Participants with comorbid asthma reported a decrease of 26 mm in VAS score for asthma symptoms. The frequency of asthma reliever medication usage was reduced or considerably reduced for 69% (n = 56) of participants who reported. Frequency was unchanged for 27% (n = 22) of participants who reported.

Conclusion: Use of MP-AzeFlu to relieve symptoms of AR decreased asthma symptoms and reduced the frequency of asthma reliever medication usage.

TP0796 | Asthma and severe obesity: Glucocorticoid sensitivity before and after bariatric surgery

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Background: Obesity has been associated with an increased asthma incidence, more frequent exacerbations and a decreased response to asthma medication such as glucocorticoids (GC). Moreover, vitamin D (vit D) deficiency has been related with worse asthma control in these patients. We hypothesized that the poor response to glucocorticoid (GC) treatment in obese asthmatic patients is due to alterations in the normal functioning of the GC receptor. Furthermore, reduced response to GC could be reversed by bariatric surgery (BS).

Method: Moderate and severe obese (body mass index [BMI] ≥35 kg/m^2) asthmatic (OA) (n = 20) and non asthmatic (O) (n = 9) patients were evaluated before BS. They were compared with non obese asthmatic patients (A) (BMI < 30 kg/m^2) (n = 9) and healthy subjects (H) (n = 15). GC sensitivity was determined *in vitro* through peripheral blood mononuclear cells (PBMCs) proliferation assay. PBMCs were incubated with a mitogenic factor for lymphocytes (PHA, 1 µg/

mL), with the presence or absence of dexamethasone (from 10^{-11} to 10^{-5}M) and/or with vit D 10^{-7} M. The cellular GC sensitivity level was expressed as the molar concentration of dexamethasone needed to suppress the 50% of the PHA-induced PBMCs proliferation (CI_{50}). Forced spirometry was realized in all groups. Participants that undergo BS will be revaluated after six months.

Results: OA patients characteristics were: 55 ± [SD]7 years, BMI 40 ± 5 kg/m^2 and FEV_1 78 ± 18% and from O patients were: 49 ± 7 years, BMI 46 ± 8 kg/m^2 and FEV_1 95 ± 12%. From A patients were: 51 ± 16 years, BMI 27 ± 8 kg/m^2 and FEV_1 93 ± 8% and H group had 40 ± 13 years, BMI 24 ± 2 kg/m^2 and FEV_1 97 ± 13%. OA patients showed the worst pulmonary function compared with other groups ($P \leq 0.05$). PBMCs from OA and O groups showed a trend to a reduced GC sensitivity compared with healthy subjects. All groups presented a significant reduction of CI_{50} values when vit D is added in the *in vitro* treatment ($P \leq 0.001$).

Conclusion: PBMCs proliferation was suppressed by dexamethasone. Vit D showed an anti-proliferative effect by itself and seems to play a relevant role in GC sensitivity in moderate and severe obese patients.

TP0797 | Bacterial lysates as add-on therapy in obstructive lung diseases: A systematic review and a meta-analysis

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Background: Exacerbations are the main cause of morbidity in obstructive lung diseases such as asthma and COPD. In a substantial number of exacerbations, respiratory viruses are involved. Bacterial lysates (BL), might prevent recurrent respiratory tract infections and therefore reduce exacerbations. BL mainly consist of inactive bacterial extracts from pathogenic respiratory bacteria and have been used from the early 50's. Moreover, immunomodulatory effects have been observed in human and animal studies. In this meta-analysis we aim to assess the effect of add-on bacterial lysate therapy on exacerbation frequency in obstructive lung diseases and discuss the underlying immunological mechanisms.

Method: We performed a systematic literature review based on the PRISMA statement and a meta-analysis using Revman_5.3. Data were estimated using mean differences (MD) and relative risks (RR). Out of 98 screened articles 24 studies were included, of which 12 provided data for a meta-analysis and 12 were suitable for systematic review; 14 clinical trials and 10 laboratory studies.

Results: Twelve articles were used for a meta-analysis. After sensitivity analysis to resolve heterogeneity, omitting 6 articles, for asthma a MD of -0.86 exacerbations (95%CI -1.21;-0.50; $P < 0.00001$) and for COPD a 23% exacerbation reduction (RR 0.77; 95%CI -0.68;-0.88; $P = 0.0002$) was calculated *(table 1)*. In animal studies a significant reduction of eosinophils was described combined with a reduction of several serum cytokines such as IL-4, IL1β, IL-5, IL-13 and TGFβ and an increase of IL-10 and IFNγ. Four studies reported similar immunological effects of BL in human serum; a significant decrease in IL-4 and an increase of serum IL-10, IFNγ, and NKT $CD4^+$cells.

Conclusion: Bacterial lysates can be considered as add-on therapy in adults with obstructive lung diseases such as asthma and COPD to prevent recurrent exacerbations, most likely through Treg differentiation and Th2-cytokine downregulation.

TABLE Exacerbation frequency with BL or placebo

Studies asthma	Mean (SD) BL	Total BL users	Mean (SD) Placebo	Total Placebo users	Mean Differences [95% CI]	Studies COPD	Mean (SD) BL	Total BL users	Mean (SD) Placebo	Total Placebo users	Relative Risk [95% CI]
Emeryk (2018)	1.1(1.3)	74	1.9(2.0)	76	-0.80[-1.34,-0.26]	Braido (2015)	43	146	41	142	1.02[0.71, 1.46]
Lu (2015)	0.9(0.7)	24	1.8(1.2)	36	-0.90[-1.38,-0.42]	Cazzola (2007)	21	33	23	30	0.83[0.60, 1.15]
						Soler (2007)	96	142	121	131	0.73[0.65, 0.83]
						Tang (2015)	45	192	64	192	0.70[0.51 ,0.97]
Total		98		112	-0.86[-1.21,-0.50]	Total	205	513	249	495	0.77[0.68, 0.88]

Registered with Prospero: CRD42017078141

TP0798 | Exercise and physical activity impact on the allostatic load: Evidence from a two steps clinical trial

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Background: Allostatic load index (ALI) measures physiologic responses to stress and is based on a compose score of biomarkers which have been associated with several diseases, including asthma. The effect of acute dietary or physical activity changes on allostatic state are unknown. Therefore, we aimed to assess the impact of a Mediterranean (MdM) versus a fast-food type meal (FFM) meal- exercise challenge (EC) as well as the effect of acute reduction of physical activity on ALI.

Method: This is a two steps clinical trial: (a) randomized crossover clinical trial, comparing the effect of a FFM versus an isoenergetic similar MdM followed by an exercise challenge (EC); and (b) before and after study evaluating the effect of decreasing by half the usual physical activity level, monitored by number of steps/day, during 2 weeks. ALI was evaluated before and after each meal, EC and after physical activity reduction. It included 18 parameters from 5 domains: cardiorespiratory (SBP, DBP, FEV1 and heart-rate); neuroendocrine (cortisol; DHE-S, epinephrine; norepinephrine), immune (High sensitivity C-reactive protein), metabolic (HDL, LDL, total cholesterol, triglycerides, glucose and insulin) and anthropometric (body mass index, fat-free mass and total body water). Biomarkers were divided in-population specific quartiles (≥75th percentile were assigned a score of 1, except for HDL, FEV1 and total body water where the lowest quartile ≤ 25 percentile was used). A total of 46 participants (26 females), median aged 25 years, 28% with asthma were included; 39-completed protocol, 29 reached more than 30% reduction on physical activity. Paired sample t-test were used for comparison.

Results: Acute exercise challenge, independently of the previous meal, induced a significant increase of the allostatic load index [mean(sd): 2.43(1.62) and 2.38(2.24) after MdM-EC and FFM-EC, respectively]. Also, reducing physical activity lead to an increase of allostatic load index from 5.10(1.87) to 6.43(2.12), $P < 0.001$. Different meals did not affect the allostatic state [0.41(1.32) MdM and 0.35(1.99)FFM].

Conclusion: Allostatic state was significantly modulated by an acute exercise challenge, independently of the meal type, and by acute decrease in physical activity levels. The impact of these stressors in the allostatic state should be considered in exercise practice as they might contribute to allostatic overload.

TP0800 | Clinical characteristics of patients with AERD and eligibility for therapy with monoclonal antibody in a Brazilian cohort

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Background: Aspirin-exacerbated respiratory disease (AERD) is a syndrome that includes eosinophilic asthma, chronic rhinosinusitis, recurrent nasal polyps, hypersensitivity to nonsteroidal anti-inflammatory drugs (NSAIDs). AERD may be an endotype of severe asthma. However, with the advent of monoclonal therapy, classifying these patients based on their phenotypes would evaluate the prospect of responding to these new drugs. The aim of this study was to identify the AERD phenotypes and to describe the proportion of these patients eligible for targeting IgE or IL-5.

Method: Retrospective study of AERD patients followed-up at the asthma outpatient clinic of a tertiary hospital. All patients were adults, had nasal polyposis, rhinosinusitis, asthma, history of hypersensitivity to NSAIDs and sporadic acute exacerbation. Demographic characteristics, asthma severity, peripheral eosinophilia, total IgE and specific IgE for aeroallergens were analysed. Patients were classified according to the current inclusion criteria in the package insert for the use of monoclonal therapies (anti-IgE, anti-IL-5 or anti-rIL-5).

Results: Sixty-one patients were included. Twenty-five patients (40.9%) were atopic. Women were more frequent in both groups, atopic and nonatopic, as well as mean age. Patients with atopic asthma had earlier age at onset of asthma (25 versus 38 years, $P = 0.006$) and more severe asthma (88% versus 53%, $P = 0.027$). Aspirin and dipyrone were the more frequent eliciting drugs. The mean total IgE was 527.9 IU/mL and eosinophils, 638.8 cell/mm3. Classifying these patients for anti-IgE monoclonal therapy, only 19 patients would receive this drug, 9 patients would be excluded due to total IgE, 18 due to non-severe asthma and 36 to nonatopic asthma. For anti-IL-5 or anti-rIL-5, 34 patients would receive this drug, 18 patients would be excluded due to non-severe asthma and 12 due to eosinophils < 300 cell/mm3.

Conclusion: DREA is characterized by severe asthma and an eosinophilic inflammatory profile, being more frequent in women and nonatopic patients. This study showed that, according to current indications in the leaflet, a greater number of patients would receive anti-IL-5 or anti-IL-5r treatment due to the high frequency of peripheral eosinophilia and, on the other hand, a large number of nonatopic patients would not receive anti-IgE treatment.

Aspirin-exacerbated respiratory disease (AERD) is a syndrome that includes eosinophilic asthma, chronic rhinosinusitis, recurrent nasal polyps, hypersensitivity to nonsteroidal anti-inflammatory drugs

(NSAIDs). AERD may be an endotype of severe asthma. However, with the advent of monoclonal therapy, classifying these patients based on their phenotypes would evaluate the prospect of responding to these new drugs. The aim of this study was to identify the AERD phenotypes and to describe the proportion of these patients eligible for targeting IgE or IL-5.

TP0801 | Overlap of the indication of biological therapy in severe asthma according to the prescription data sheets

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Background: Treatment of severe asthma with biologicals is chosen according to biomarkers: total IgE (omalizumab) and/or eosinophils (mepolizumab, reslizumab, benralizumab). However, there is a certain degree of overlap in the indication of these biologicals based on their prescription data sheets. It has been reported that at least 30-40% of patients with severe asthma show both: respiratory allergy and eosinophilia (300 cells/μL). In this study, we evaluated patients on treatment with omalizumab who met criteria for treatment with mepolizumab and, conversely, patients with mepolizumab who could be treated with omalizumab.

Method: We performed a retrospective descriptive analysis of patients who were treated with omalizumab or mepolizumab since 2006 due to severe asthma. Demographic, clinical, analytical and therapeutic data were collected from the electronic medical records.

Results: Twenty-nine patients (female 65.51%), mean age 45.34 years (24-71), diagnosed with severe asthma were treated with omalizumab: 27 (93.10%) associated respiratory allergy, mean total IgE levels were 440.97 kUA/L (24-1630) and mean eosinophil count in peripheral blood 0.72 cells/μL (0.1-1.28).

Thirteen patients (female 76.92%), mean age 59.23 years (51-75), were treated with mepolizumab: 6 (46.15%)with respiratory allergy, mean total IgE levels 304.62 kUA/L (23.9-884) and mean eosinophil count in peripheral blood was 1.39 cells/μL (0.35-3.38).

According to the prescription data sheets of the anti-IL5 biologicals, 20 patients (68.96%) treated with omalizumab could have been treated with either mepolizumab or benralizumab (eosinophils in peripheral blood > 300 cells/μL), and 18 (62%) with reslizumab (eosinophils in peripheral blood > 400 cells/μL).

According to the prescription data sheets of omalizumab, 6 patients (43.15%) treated with mepolizumab could have been treated with omalizumab, although only 4 of them did it.

Conclusion: The majority of severe asthma patients who were treated with monoclonal antibodies showed respiratory allergy and eosinophilia. In this group of patients, the choice of a biological therapy was based on additional criteria, as the use of biomarkers to predict the response to targeted therapies do not show an optimal specificity.

SUNDAY, 2 JUNE 2019
TPS 11
ASTHMA: MANAGEMENT

TP0802 | Compliance with home nebulizer therapy and asthma control level in a cohort of asthmatic children: First survey in China

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Background: Asthma control level and treatment compliance vary widely around the world. Studies have demonstrated a relatively low asthma control level and treatment compliance in China. This study aimed to evaluate patients' compliance with home nebulizer therapy and influential factors in Chinese asthmatic children.

Method: This study (NCT03156998) was a multicenter, prospective and observational study of asthmatic patients under 14 years old who have been prescribed home nebulization treatment for three months from June 2016 to June 2018. Eligible patients were enrolled consecutively from 12 Tier 3 hospitals across the region of Northern, Southern, Western and Eastern in China. Data including demographics, symptoms, medications, exacerbations and health economic information, etc. were collected using CRFs (Case Report Forms). Actual frequency of patients' nebulization treatment was recorded by electronic chips embedded in nebulizer and meanwhile reported by care giver through patient's diary. The compliance with nebulization treatment was derived using actual frequency divided by prescribed frequency of treatment.

Results: 510 patients (99.6%) were included into Full Analysis Set (FAS) of 512 successfully enrolled patients. The mean age (± SD) of FAS population was 3.53 (± 2.42) with 343 (67.4%) of them were male. The median compliance rate monitored by electronic chips was 69.91% and the median compliance rate reported by caregivers was 77.93%. The patients with well-controlled asthma was only 12.01% at baseline, then increased to 54.44%, 67.02% and 77.47% after 1, 2 and 3 months treated with nebulization budesonide therapy, respectively. The length of asthma history remained statistically significant in multivariate analysis that longer disease history increased the probability of better compliance ($P = 0.0138$).

Conclusion: These results demonstrate that three months compliance with home nebulizer therapy for Chinese asthmatic children is good. Asthma control levels improved with the extension of treatment. Home nebulizer therapy is an alternative treatment for children with asthma in China.

TP0803 | Efficacy of mepolizumab in severe eosinophilic asthma by baseline eosinophil count and exacerbation history: Meta-analysis of two phase 3 trials

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Background: Mepolizumab is approved as add-on therapy in patients with severe eosinophilic asthma (SEA) and Phase 3 clinical trials have consistently demonstrated reduced rates of exacerbations compared with placebo. We assessed the efficacy of the licensed 100 mg subcutaneous (SC) dose of mepolizumab in patients with SEA by baseline blood eosinophil count (BEC) and number of exacerbations in the prior year.

Method: This was a post hoc inverse-variance fixed-effects meta-analysis of the Phase 3 randomised, controlled trials MENSA & MUSCA. Patients with SEA (BEC: ≥150 cells/μL at baseline or ≥ 300 cells/μL in previous year) received mepolizumab 100 mg SC or placebo for 24 (MUSCA) or 32 (MENSA) weeks. The primary endpoint was the annualised rate of clinically significant exacerbations (CSEs); this was assessed by baseline BEC (<300, ≥300, <400, ≥400 cells/μL) and number of exacerbations in the prior year (≥2, <3, ≥3, ≥4) using negative binomial regression.

TABLE 1. Ratio of the annual rate of CSEs by baseline BEC and exacerbation history

BEC (cells/μL) + exacerbations	Exacerbations in prior year	Rate ratio (95% CI) mepolizumab/placebo
<300	≥2	0.66 (0.48, 0.91)
≥300	≥2	0.37 (0.28, 0.50)
≥300	≥3	0.31 (0.21, 0.44)
≥300	≥4	0.28 (0.18, 0.44)
<400	<3	0.59 (0.37, 0.92)
<400	≥3	0.63 (0.43, 0.91)
≥400	<3	0.36 (0.21, 0.62)
≥400	≥3	0.29 (0.19, 0.43)

Results: Of 936 patients included, 468 received mepolizumab and 468 placebo. Mepolizumab reduced CSEs by 34%-72% versus placebo (Table 1); the greatest reduction was seen in patients with BEC ≥ 300 cells/μL and ≥ 4 exacerbations in the prior year.

Conclusion: Baseline BEC is associated with the impact of mepolizumab on exacerbation rate reduction.

Funding: GSK (meta-analysis:208115 [studies:115588/NCT01691521;200862/NCT02281318]).

TP0804 | Adverse events of high dose of inhaled corticosteroid for patients with severe asthma

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Background: Inhaled corticosteroids (IC) at high doses associated with the long-acting bronchodilator (LABA) is currently the main treatment for severe asthma control. Another criterion for diagnosis of severe asthma is the use of systemic corticosteroids (CS) for more than 50% of the previous year. The aim of this study was to evaluate the adverse effects of high dose IC in patients with severe asthma accompanied in a tertiary service.

Method: Retrospective study of electronic medical records of adult patients diagnosed with severe asthma in follow-up at a tertiary hospital. Patients using ICs (budesonide) > 1000 mcg/day for more than 1 year were included. Patients were assessed for demographic data, IC dose, use of associated systemic corticosteroids, atopy, forced expiratory volume in the first second (FEV1), serum immunoglobulins and serum cortisol.

Results: Eight-one patients were evaluated, being 82.7% females, mean age 57.1 years and age of onset of asthma of 17.1 years. The mean IC dose was 1681.5 mcg/day and 28.4% of the patients had used CS for a prolonged period. Regarding the exams: atopy was present in 67.9% of the patients, mean FEV1 was 59.8%, mean serum IgG was 961.0 mg/dL and IgE was 402.8 IU/mL. Hypogammaglobulinemia (IgG < 500 mcg/dL) was observed in 6.3% of the patients. Thirty-six patients (55.4%) had a serum cortisol reduction (<5.4 μg/dL) at some time during follow-up, and 66.7% of these patients had not used CS for prolonged periods.

Conclusion: With the introduction of IC associated with LABA for the treatment of asthma there was a significant reduction in the frequency of exacerbations, hospitalizations and side effects associated with CS. However, IC may also be associated with side effects that need to be monitored, such as those observed in this study, hypogammaglobulinemia and reduced serum cortisol.

TP0805 | Assessment of the functional status and application of long-acting m-anticholinergic in children with bronchial asthma in real clinical practice

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Background: The long-acting M-anticholinergic Tiotropium Respimat is additional therapy drug in patients with bronchial asthma (BA), which is not achieved on the BA control in monotherapy inhaled corticosteroids (ICS) or their combination with long-β2-agonists (ICS/LABA). Aim: To assess the change in the functional status of children with BA after treatment with Tiotropium Respimat for 3 months in real clinical practice.

Method: The observational study included 12 children aged 6-11 years, suffering from moderate and severe BA with insufficient BA control in monotherapy with ICS in medium/high doses or a combination of ICS/LABA in medium/high doses. These patients added Tiotropium Respimat at a dose of 5 μg /day. The efficiency was assessed by monitoring the peak expiratory flow rate (PEF), of forced expiratory volume in 1 second (FEV_1) before bronchodilator, BA symptoms, the need for short-acting bronchodilators (SABA), and the number of exacerbations. BA control and quality of life were assessed using questionnaires (ACT, ACQ and AQLQ - respectively).

Results: On visit 1: PEF, % 54.8 ± 1.7; daily variation of PEF,% 35.3 ± 2.3; FVC,% of the proper of 58.4 ± 9.6; FEV_1, % 62.3 ± 4.7; FEV_1(mean, liters)1629, an increase of the maximum FEV_1 (mean, liters) + 0.263. Daytime symptoms/week in points 4.7 ± 2.9; nocturnal symptoms in points 3.2 ± 2.1. Reliever need/week 6.2 ± 3.9. Median ACT score 19 (16-23) (from 0 to 25). Mean ACQ total score 2.71 ± 1.9 (from 0 to 6). Mean AQLQ total scores (from 1 to 7) were 5.31 ± 1.05 for controlled patients, 5.01 ± 0.68 for partially controlled and 4.03 ± 0.35 for uncontrolled patients according to ACT ($P < 0.001$). For 2 visits (after 3 months later): PEF, % 92.5 ± 2.7; daily variation of PEF,% 7.8 ± 1.6; FVC,% of the proper of 84.2 ± 7.2; FEV_1, % 80.4 ± 2.6; FEV_1(mean, liters) 2869, an increase of the maximum FEV_1 (mean, liters) + 0.422. Daytime symptoms/week in points 1.4 ± 2.1; nocturnal symptoms in points 1.0 ± 0.9. Reliever need/week 2.2 ± 1.8. Median ACT score 21 (19-25). Mean ACQ total score 2.71 ± 1.9. Mean AQLQ total score±SD 5.65 ± 0.49. Exacerbations of the disease during the period of observation was not noted. No adverse events were observed. At the same time, therapeutic success was achieved in therapy without increasing doses of ICS for each patient.

Conclusion: In children with moderate and severe BA Tiotropium Respimat (5 μg), when added to maintenance therapy, improves lung function and quality of life, reduces the severity of symptoms and the frequency of exacerbations.

TP0806 | Efficacy of omalizumab after 16 weeks treatment in a severe cortico dependent eosinophilic non-allergic asthma

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Case report:

Introduction: Nowadays there is no currently labeled indication of Omalizumab treatment for severe non-allergic asthma. Also there are nonconclusive studies of this anti-IgE treatment efficacy in non atopic, non allergic, intrinsic severe asthma, despite well recognized positive outcomes in extrinsic allergic asthma. Severe asthma is a subset of difficult-to-control asthma; the term is used to describe patients with asthma that remains uncontrolled despite treatment with high-dose inhaled glucocorticoids combined with a long-acting β2-agonist (LABA), a leukotriene modifier, or theophylline for the previous year or treatment with systemic glucocorticoids for at least half the previous year.

Case report: We aim to present the case of one 38 years old female suffering from persistent perennial productive cough, severe dyspnea, wheezing, from 2 years attributed to GERD and non improved by PPIs. Since age of 15th years patient had perennial oculorhinitis and nasal obstruction which has been followed by ethmoidectomy, but with partial benefits. Latter performed examinations showed following results: Blood count (leucocytes = 11.51 x 103; hypereosinophilia 15%); total IgE = 689 IU/mL; negative prick tests and sIgE for pneumo and tropho allergens; normal ranges of sIgE for H. Pyloris and Asperligus Fumigatus. ANA, ANCAp, ANCAc serum levels were also normal. BAL showed hypereosinophilia; Toracal CT: Bilateral bronchiectasis; Cranial CT: Hypodens material in all paranasal sinuses. Spirometry: FEV1/FVC = 64.64%; We concluded the diagnosis of Severe Intrinsec Eosinophilic Asthma and started treatment with montelukast, LABA, high dosage corticosteroids up to 80 mg, but patient had mild improvement in several months. Lowering in cortisone dosage caused severe clinical exacerbations. Facing the situation with presented clinic conditions and persistent high levels of eosinophilia and tIgE level the decision to put the patient on omalizumab treatment has been taken. Treatment with 350 mg omalizumab every 2 weeks for 16 consecutive weeks has been subcutaneous administered. Following 16 weeks of treatment patients has shown significant clinical improvement, has lowered cortisone dose up to 4 mg/day and reached FEV1/FVC = 87.12%.

Conclusions: This is first case in our clinic of eosinophilic severe non allergic asthma treated with omalizumab, presenting very good clinical outcomes after treatment.

TP0808 | Allergic bronchopulmonary aspergillosis (ABPA) and omalizumab treatment

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Background: Standard treatment for ABPA includes systemic corticosteroids and oral antifungal agents. The role of omalizumab treatment in ABPA is not firmly established; however, some recent studies have demonstrated clinically and statistically significant reductions in exacerbations. We present a clinical case successfully treated with omalizumab.

Method: A 65- year-old house wife diagnosed of non allergic mild-moderate perennial asthma since 2007, attended our outpatient consult referring persistent severe asthma not controlled with montelukast, aclidinium and formoterol+beclomethasone 200/6 every 8 h. She also had suffered *Klebsiella pneumoniae* exacerbations in 3 occasions and peripheral bronchiectasis. Since her baseline total IgE was 2153 KU/L (ImmunoCAP), we performed skin prick test to molds, specific *Aspergillus* IgE and IgG, *Aspergillus* precipitins, spirometrical monitoring and high resolution thoracic CT.

Results: The skin prick test performed to *A. fumigatus*: positive (5 × 6 mm). Specific *Aspergillus* IgG: 42.5 mg/L, specific IgE *Aspergillus*: 12.1 KU/L, r Asp f 6: 1.66 KU/L. Blood eosinophilia: 380 mm^3, *Aspergillus* precipitins negative. Spirometric decline from mean baseline FEV1 75% of predicted to 61%.

The total IgE level decreased after starting oral steroids and itraconazole in October 2016 with clinical improvement until June 2018 (809 KU/L), when IgE levels increased progressively and we stopped the reduction of oral corticosteroids (prednisone 25 mg alternating days). Omalizumab 600 mg/15 days was then started and corticosteroids were latter ceased, 7 months later. All along the treatment with oral corticosteroids the patient has undergone the onset of diabetes mellitus, poor regulation in blood pressure, temporary iatrogenic Cushing syndrome and multiple sputum infections with different bacteria: *K pneumonia*, *E coli*, *St aureus*, *Ps aeruginosa*, *Enterobacter cloacae*, *Acinetobacter*... that were treated with antibiotics according to antibiogram.

The patient remains stable nowadays without exacerbations with a maintenance dose of 600 mg of omalizumab monthly. ACT score and FeNO show improvement with this treatment. Thoracic CT scan revealed reduced inflammation of the distal airways.

Conclusion: We describe a new case of serologic ABPA treated with omalizumab due to the partial response to oral corticosteroids. We consider that add-on omalizumab is an effective and well tolerated treatment in our patient with severe ABPA.

TP0809 | Patient-physician discordance in the assessment of adherence to inhaled medication

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Background: Assessing adherence to inhaled medication remains a challenge in clinical practice. This study compared patient's and physician's assessment of inhaled medication adherence and identified predictors of discordance between those assessments.

Method: Adults and adolescents with persistent asthma were recruited at 29 allergy, pulmonology and paediatric secondary care outpatient clinics, in the context of two observational prospective studies of the INSPIRERS project. Patients and physicians independently rated adherence to inhaled medication during the previous week, using a 100-mm visual analogue scale (VAS). Demographic and anthropometric characteristics, patients' follow-up time, asthma characteristics and control according to GINA and current treatment were collected. VAS scores and categories (0-50, 51-80, 81-100) were used in the analyses. Discordance was defined as VAS scores difference-VAS-d ≥ 10 mm or classification in distinct categories. Correlations with Spearman's rho (r_s) were used to explore the association between patients' and physicians' VAS scores and kappa to determine the agreement between categories. Multivariable logistic regression analysis was used to identify predictors of discordance (VAS-d ≥ 10 mm).

Results: A total of 395 patients (61% female; 68% adults), with a median (interquartile range-IQR) age of 28 (16-46) years were analysed. Inhaler adherence was rated as high both by patients (median-M 85 mm, IQR 65-95) and physicians (M 84 mm, IQR 68-95) ($P = 0.707$), with a median VAS-d of 10 mm (IQR 4-20). Correlation between patient and physician VAS scores was moderate ($r_s = 0.58$; $P < 0.001$). Using VAS-d ≥ 10 mm, patients and physicians disagreed in 53% of cases, with physicians overestimating adherence in 26%. Using VAS categories, disagreement occurred in 36% of cases (kappa = 0.4; 95%CI 0.32-0.48), and physicians overestimated adherence in 17%. Absence of asthma control (odds ratio-OR 3.05, 95% CI [1.59-5.89]) and short-acting β2-agonist prescription (2.69 [1.22-5.92]) were associated with increased discordance, while having a written asthma action plan (0.38 [0.20-0.74]) and hospital admissions in the past year (0.13 [0.03-0.52]) were associated with reduced discordance ($R^2 = 20\%$).

Conclusion: Patients' and physicians' assessment of inhaler adherence were discordant in more than 1/3 of cases and were only moderately correlated. The reasons for discordance need further investigation. These results highlight the shortcomings of global subjective measures of inhaler adherence.

TP0811 | Evaluation of the asthmatic children's quality of life

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Background: Asthma is one of the most frequent chronic respiratory disorders in children affecting up to 15% of children in Europe. It is manifested with chronic cough; exacerbations of wheeze, breathlessness and respiratory discomfort due to reversible bronchospasm. Most of the asthmatic patients are considered as mild; however, 5-10% of patients suffer from severe disease leading to limitation in daily activity and sleep disturbance as well as recurrent attacks. Asthma has a considerable impact on patients' quality of life especially among severe asthmatic patients. This study was designed to evaluate the quality of life in 8-12-year-old asthmatic patients.

Method: A cross-sectional study was conducted in 2017-2018 using the Persian version of PedsQL™ questionnaire. A total of 140 asthmatic patients who referred to allergy clinic in Bahonar and Children Medical Center hospitals affiliated to Alborz and Tehran University of Medical Sciences respectively, were diagnosed by an allergist with 140 healthy children as the control group were enrolled. Data were analyzed using SPSS24 and *P* value less than 0.05 was considered meaningful.

Results: More than half of the patients and control group were boys (n = 85; 58.6%). The mean total score of PedsQL™ in asthmatic group was 23.11 (SD = 15.60) comparing to 8.96 (SD = 9.89) in control group ($P < 0.001$). All different aspects of quality of life; physical performance, social function, emotional performance and performance in school were significantly lower in asthmatic group. The quality of life score was considerably lower in patients with a history of hospital admission and patients with high steps of asthma severity ($P < 0.001$). There was no significant difference in score of PedsQL™ between girls and boys ($P > 0.05$).

Conclusion: Asthma has a significantly adverse effect on different aspects of children's quality of life including physical performance, social function, emotional performance and performance in school.

TP0812 | Asthma control in real clinical practice

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Background: The goals of asthma management are to achieve good symptom control and to minimize future risks. Many patients and general practitioners (GPs) overestimate the control of asthma. The aim of this study was to assess asthma control in cross section and 1-year prospective study according to stepwise approach to treatment in real clinical practice.

Method: We examined 640 outpatients (37% male, aged 18-89 yr, mean age 44 yrs) with stable asthma referred to our secondary care center by GPs. Atopy was diagnosed in 78% patients, aspirin-induced asthma in 7%, steroid-dependent asthma – in 6%. In patients with asthma 18% were current and 23% former smokers. Concomitant allergic rhinitis was diagnosed in 82%, COPD - in 10%, obesity – in 26% of patients with asthma. Patients were treated according to GINA steps (2017). Asthma control was assessed by ACQ-5.

Results: Step-1 therapy was prescribed to 7% patients, Step-2 – to 13%, less than half of those used inhaled steroids (ICS). Step-3 medications were prescribed to 48% of asthmatic patients, Step-4 – to 21% and Step-5 to 11%. In Step-5 group 51% of patients were treated by oral steroid and 60% by biologicals. Uncontrolled asthma (ACQ-5 ≥ 1.5) was diagnosed in 57% of patients: Step-1%-20%, Step-2 – 25%, Step-3 – 57%, Step-4 – 84% and Step-5 – 79%. In 316 patients asthma control was assessed at baseline (mean ACQ-5 – 1.88, 57% with ACQ5 ≥ 1.5) and after 1 year of follow-up (ACQ-5 – 1.21, 34% with ACQ5 ≥ 1.5, $P < 0.0001$). Proportion of patients with uncontrolled asthma changed during 1 year compared to baseline: Step-1 – 19% vs 24% ($P > 0.05$), Step-2 – 11% vs 17% ($P < 0.001$), Step-3 – 27% vs 55% ($P < 0.0001$), Step-4 – 48% vs 78% ($P < 0.0001$) and Step-5 – 58% vs 75% ($P < 0.0001$).

Conclusion: Asthma control is low in real clinical practice. Some patients with mild asthma, especially at Step-1 therapy, do not reach control after 1 year of treatment and need use of ICS or increase of ICS dose. Asthma control can be achieved in 40-50% of severe asthmatics.

TP0813 | Severe asthma questionnaire: Translation to portuguese and cross-cultural adaptation for use in Portugal

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Background: The Severe Asthma Questionnaire (SAQ) is designed to measure the impact of asthma symptoms on quality of life and the impact of asthma treatments since the existing asthma specific health related quality of life scales are not optimally aimed for severe asthma patients. It produces a total domain score and a global quality of life score. The SAQ combines two parts along four pages. The first part includes 16 questionnaire items to measure the disease burden over the last two weeks in 16 different and relevant domains to severe asthma patients. Patients respond to each item by rating how difficult their disease makes that life domain on a 7-point category rating scale. The second part includes global quality of life scales to assess global quality of life during the last 2 weeks and the global quality of life during the worst and best months of the year. Preliminary data indicates that the smallest variation identified as significant (minimal clinically important difference - MCID) is 0.46 for the former and 6.0 for latter. For clinical use the questionnaire validation for the target population is mandatory. Therefore, our aim was to translate and perform a cross-cultural adaptation of SAQ so that it can be used in Portuguese patients.

Method: Based on the principles of good practice for the translation and cross-cultural adaptation of such instruments, the protocol included the following steps: acquisition of authorization from the team of the original questionnaire; translation of the instrument to Portuguese, carried out by two health professionals; reconciliation; back-translation to English, carried out by two health professionals who are fluent in Portuguese; review of the back-translation; harmonization; review and approval of the questionnaire; focus groups involving 12 patients who completed and improved the wording of the questionnaire; analysis of the results; review and preparation of the final version of the instrument approved by the original SAQ team.

Results: The final version included minor modifications suggested by the patients. The mean age of the patients was 50.08 ± 13.43 years and 50% were female. All had some level of education and the majority (58.3%) a favorable economic background.

Conclusion: The SAQ demonstrated to be comprehensible, clear, and appropriate. The original questionnaire and the Portuguese version were reliably comparable. Consequently, it can become an extensively used tool for severe asthma patients.

TP0814 | Lithuanian patient's opinion: Allergy diary MASK is user friendly

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Background: The MASK-rhinitis app (Mobile Airways Sentinel NetworK for allergic rhinitis) assesses allergic rhinitis symptoms, disease control and impact on patients' lives. A mobile phone app (the Allergy Diary) central to MASK is freely available in Lithuania. The aim: To present Lithuanian patients' opinion about the MASK allergy diary mobile app.

Method: 48 of MASK app users agreed to answer additional questionnaires about their experience. All of them had allergic rhinitis or asthma. There were 26 (54.2%) women and 22 (45.8%) men with median age 32.5 (SD 10.5) years. Patients were asked 8 questions about the satisfaction of using Allergy Diary from one to three months after the start of using this app. Four answers to each question were available (in range of completely disagree to completely agree). Responders were divided according to their age. Only 2 responders were older than 56 years old, so we divided our users accordingly: first group N 28 (18-34 years) and second – N 20 (older than 34 years).

Results: 96.4% (n = 27, I gr.) and 100% (n = 20, II gr.) of patients rated that the app was user friendly. 89.3% (n = 25, I gr) and 65% (n = 13, II gr) of respondents stated that the app was working properly and running smoothly. 96.5% (n = 27, I gr) and 85% (n = 17, II gr) patients were clearly provided with information and 82.1% (n = 23, I gr) and 95% (n = 19, II gr) liked the design of application. The software met expectations and needs of 78.5% (n = 22, I gr) and 80% (n = 16, II gr) users. 64.3% (n = 18, I gr) and 70% (n = 14, II gr) liked to use the app. 35.7% (n = 10, I gr) and 40% (n = 8, II gr) claimed that their allergy has being treated more successfully. Only 15% (n = 3) of older age group did not think that app helped to treat their allergy more successfully and they would prefer to see doctor face to face. However, 92.9% (n = 26, I gr) and 95% (n = 19, II gr) of respondents would recommend application to people with allergy.

Conclusion: Lithuanian patients evaluated the MASK allergy diary as simple to use and meeting their expectations.

TP0815 | Asthma control test reflects not only lung function but also airway inflammation in stable asthma of children

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Background: Various numerical asthma control tools have been developed to provide scores and cut points to distinguish different levels of symptom control. We aimed to examine whether asthma control test (ACT) can reflect objective findings such as lung function, fractional exhaled nitric oxide (FeNO), and laboratory data in stable asthma.

Method: We included patients who were enrolled in Korean Childhood Asthma Study. ACT, spirometry, blood tests, FeNO were performed when asthma was stabilized. We examined the differences in various parameters of spirometry, blood tests, and FeNO depending on control status determined by ACT and whether any correlation existed.

Results: The study population consisted of 441 subjects. In regards to asthma severity, 184 patients were with mild intermittent, 154 were with mild persistent, 97 were with moderate persistent, and 1 was with severe persistent asthma. In spirometry, forced expiratory volume in one second (FEV_1), forced expiratory flow between 25%-75% of forced vital capacity, FEV_1/forced vital capacity was significantly higher in the controlled group. FeNO and % change in FEV_1 was significantly lower in controlled group. In blood tests, eosinophil fraction was significantly lower in controlled group while white blood cell count was significantly higher in controlled group. We examined if any correlation could be found between ACT scores and various factor but only provocative concentration of methacholine causing a 20% fall in FEV_1 showed significant correlation with ACT score.

Conclusion: ACT can be useful as a part of the routine evaluation of asthmatic children, as a complement to other tools, such as spirometry and FeNO measurement.

TP0816 | National program of asthma management in the Republic of Kazakhstan

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Background: The illnesses of respiratory system, including pneumonia, asthma, bronchitis, and emphysema have taken first place in the structure of diseases of the Republic of Kazakhstan involving 2.5 million patients. Asthma morbidity is growing from year to year. There are 43.9 patients with bronchial asthma per 100 000 population in Kazakhstan, the prevalence in children aged 0-14 years is 64.8. Each year there is an increase in bronchial asthma from 10-15%.

Method: A National Program for asthma management was first created in 1998 in Kazakhstan, and renewed in 2005, 2007 and 2011. Costs of asthma treatment in Kazakhstan are covered from Government budget - basic and emergency help is free for patients. Basic treatment included inhaled steroids in monotherapy (mometasone furoate, budesonide, fluticasone furoate, ciclesonide) or combinations of inhaled corticosteroids with long-acting B2 agonist (fluticasone in combination with salmeterol or budesonide in combination with formoterol) (mometasone furoate with azelastine and montelukast) and montelukast. Emergency drugs included salbutamol. Our objective was to investigate effectiveness of asthma management.

Results: 133 patients 5-60 years old who received combination of fluticasone and salmeterol or budesonide plus formoterol were under observation. After achieving control in 2 months, treatment was changed into inhaled steroids in monotherapy. Patients with virus-induced asthma were treated with the addition of montelukast to basic therapy. Patients with severe allergic asthma received omalizumab treatment. Further allergen-specific immunotherapy was performed in allergic asthma and full control was achieved with sustainable remission.

Conclusion: The work of National Program for asthma management allows treating asthma patients more effectively.

TP0817 | Patients education and adherence to treatment in management of bronchial asthma

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Background: Improvement of the adherence to treatment and its maintenance at a high level is one of the main issues of the asthma management nowadays. Complex training program can be a key tool in the adherence improvement.

Method: 68 patients with partly controlled moderate and severe bronchial asthma were involved in the study, including 23 men and 45 women. All patients used dry-powder inhaler previously. Every patient was educated to the proper technique of inhaler use before the treatment initiation. Education included printed instruction, educational video and demonstration of the inhaler use by the specialist. Correctness of the inhaler use was assessed after the completion of education and at each visit of the patient. ACQ-5 questionnaire score, forced expiratory volume in 1 second (FEV1), adherence to treatment by self-report and dose meter, correct Easyhaler using technique, satisfaction with inhaler use were assessed at the beginning and 8 weeks after the treatment initiation. Satisfaction with the inhaler use was measured from 0 (completely unsatisfied) to 5 (completely satisfied).

Results: Before the treatment initiation ACQ-5 score was 2.51 ± 0.20, after 8 weeks of treatment it was 1.43 ± 0.19 degrees (P = 0.033). Adherence to treatment increased from 51.3%±5.4% to 80.1%±8.7% (P = 0.024), FEV1 increased from 53.1 ± 6.7% to 63.8%±7.1% (p-0.041), satisfaction with inhaler use increased from 3.2 ± 0.4 to 4.4 ± 0.6 (P = 0.042). Number of patients, who used Easyhaler correctly increased from 24 (35.3%) at initial point to 62 (91.2%), P < 0.001. Exacerbation rate was 0.36 ± 0.05 and 0.32 ± 0.05 (P > 0.05), that is probably due to short period of observation.

Conclusion: Complex training with Easyhaler use reliably increase adherence to BA treatment, results of ACQ-5 questionnaire, FEV1, improve technique of delivery device using, satisfaction with inhaler use. The exacerbation number has not changed during 8 weeks of observation.

TP0819 | Tidal changes in respiratory reactance are sensitive indicators of airway obstruction in severe asthma

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Background: The forced oscillation technique(FOT) is a noninvasive method with which to measure respiratory system resistance(Rrs) and reactance(Xrs) during tidal breathing. Recently, the clinical application of FOT as a measurement of the lung function has progressed, and an increasing number of reported studies have examined its usefulness in the evaluation or management of obstructive lung diseases, including asthma and chronic obstructive pulmonary disease (COPD). Studies in asthmatics have demonstrated efficacy in detecting airway obstruction, bronchodilator response and changes in parameters against bronchoprovocation stimuli. There is evidence that the method is more sensitive than spirometry, with the ability to detect changes earlier, even in asymptomatic individuals whose FEV1 is normal. Aim: To evaluate the pulmonary function of patients with childhood-onset severe asthma through respiratory impedance(Zrs) measurements and to verify diagnostic accuracy.

Method: Cross-sectional, exploratory study. The sample consisted of adults with clinical diagnosis of severe asthma(SA) and healthy adults(HA). The SA group was divided into two subgroups: severe asthma refractory(SAR) and severe asthma no refractory(SANR). The patients with SAR received omalizumab. The asthmatic patients underwent clinical evaluation, anthropometric measures and pulmonary function(spirometry and FOT).

Results: Ninety adults were evaluated, being 30 HA, 30 SAR and 30 SANR. Mean age in years in HA was 58.8 ± 8, 53.1 ± 11.9 in SAR and 60.2 ± 11.6 in SANR. There was a predominance of females in all three groups. The SA group had symptoms, on average, for more than 30 years, with a remission period in 33.3% of SAR and 23.3% of SANR. The median age at onset of asthma symptoms was 5a in SAR and 14a in SANR. In relation to the FOT variables, in the spectral phase: Rrs6:HA(3.3 ± 1.2), SAR(6.6 ± 2.1), SANR(7.1 ± 2.9); Xrs6:HA(-0.7 ± 0.4), SAR(-4.1 ± 2.5), SANR(-4.5 ± 3.4). Impedance analyzes, in the temporal phase of FOT, did not show a difference between SAR and SANR when comparing mean values of Rrs and Xrs, during inspiration and expiration, but distinguished asthmatics from healthy individuals. The sensitivity and specificity of reactance variable at the end of forced expiration, obtained through ROC analyses, was 100% and 96%, respectively.

Conclusion: A within-breath reactance measurement could be a potentially useful indicator of the presence of tidal expiratory flow limitation in severe asthma.

TP0820 | Comparison of responses to nasal and whole lung allergen challenges in mild allergic asthmatic subjects with allergic rhinitis

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Background: Allergen challenge to the upper or lower airways induces acute IgE-mediated allergic responses as measured by change in peak nasal inspiratory flow (PNIF) and forced expiratory volume in 1 sec (FEV_1), respectively. Late responses develop only in some individuals and are driven by T cell activation resulting accumulation of inflammatory effector cells. This study examined allergen-induced responses in the nose and lungs to determine whether development of late responses is consistent within the same individuals.

Method: Subjects with mild allergic asthma (FEV_1 ≥70% predicted, skin prick test +ve) and a history of allergic rhinitis underwent a cross-over study, undergoing whole lung and nasal challenge with matched allergen extracts. Challenges were separated by at least 4 weeks. Allergen was delivered to the lungs using a Wright nebulizer, nose clips, and through a mouthpiece in doubling doses until FEV_1 fell by 20%. Allergen was delivered to the nose using Aptar nasal spray pump and 0.1 mL/nostril in quadrupling doses until PNIF fell by 60%. Responses to allergen were followed until 7 hrs, and the kinetics and magnitude of change were compared between lung and nasal challenges.

Results: Eleven subjects completed both challenges. Compared to pre-challenge, the early (<2 hrs) and late (2-7 hrs) mean (SD) fall in FEV_1 post-lung allergen challenge was 29.5% (8.6) and 12.9% (9.5), respectively, and the fall in PNIF post-nasal challenge was 66.5% (25.2) and 47.6% (18.9), respectively. The early fall in FEV_1 and PNIF followed a similar timeline with maximum fall between 15 and 30 min. The late fall in FEV_1 occurred consistently 6-7 hrs post-lung challenge. In contrast, the late fall in PNIF was variable between subjects with the lowest average value at 2 hrs post-nasal challenge and remained low until 6 hr. There was no correlation between maximum

% fall in FEV_1 and maximum % fall PNIF during the period 2-7 hrs post-challenge.

Conclusion: The onset and duration of the allergen-induced early responses in the upper and lower airways as measured by change in FEV_1 and PNIF, respectively had a similar time course, suggesting the same cells and mediators are driving the early response in the nose and lungs. The FEV_1 and PNIF measured 2-7 hrs after challenges demonstrated that the late response in upper and lower airways is not similar in terms of magnitude, onset, or duration. This dissimilarity may be in part due the extent of airway secretions their differential effect on the two measurements.

TP0821 | Exercise-induced bronchospasm in children: Which test to choose?

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Background: Exercise is an important cause of asthma exacerbation among pediatric patients with partly controlled or uncontrolled asthma – who, according to consensus, are to be diagnosed as exercise induced bronchospasm (EIB) with asthma. Patients with acute airflow obstruction provoked by exercise but without asthma symptoms can be diagnosed as EIB without asthma, since EIB is a distinct form of airway hyperresponsiveness. The aim of this study was to compare methacholine challenge test (MCT) and exercise challenge test (ECT) results in diagnosis of EIB children.

Method: This cross-sectional study comprised 104 consecutive patients without previous asthma diagnosis ([NA], n = 55), or with partly controlled asthma ([A], n = 49), who were complaining of asthma-like symptoms triggered by exercise. Methacholine challenge test and exercise challenge test were performed in all patients, according to established protocols. For the assessment of MCT and ECT as predictor of EIB, receiver operating characteristic (ROC) curves were calculated. Areas under the ROC curves (AUC) with 95% confidence intervals (CI) and their differences from 0.5 were calculated. Sensitivities, specificities, positive (PPV) and negative (NPV) predictive values, positive (LR+) and negative (LR-) likelihood ratios were calculated for the optimal cut-points. The data were analyzed using STATISTICA version 10 (StatSoft, Inc. Tulsa, OK) and MedCalc version 12 (MedCalc Software, Mariakerke, Belgium). Statistical significance was set to $P < 0.05$ for all tests.

Results: Among 104 patients recruited (mean age: 12.98 ± 2.93 years, ranged 6-18 y.o., 46 boys), 49 (47.1%) had previously been diagnosed with asthma. BHR was confirmed in 83 (79.8%) children. ECT detected BHR in 30 (28.8%) patients, while MCT confirmed BHR in 81 (77.9%) patient. Using ROC curve analysis, MTC showed an AUC of 0.976 (95% CI 0.923-0.996), with 95.12% sensitivity and 100% specificity for diagnosis of BHR in children. However, ROC curve analysis for ECT showed an AUC of 0.630 (95% CI 0.524 to 0.728), with 26% sensitivity and 100% specificity.

Conclusion: Due to its high sensitivity, MCT is the diagnostic test of choice for confirmation of EIB in children.

SUNDAY, 2 JUNE 2019
TPS 12
CELLULAR MECHANISMS OF AUTOIMMUNITY

TP0822 | Inaugural hereditary angioedema in a child

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Case report: Hereditary angioedema due to C1-inhibitor deficit is an autosomal dominant disease with an estimated prevalence of 1:50 000. Mean age at the beginning of symptoms is 11.2 years-old, although starting on the first decade of life is not uncommon. Even though family history typically suggests the diagnosis, sometimes atypical presentation or negative family history may delay diagnosis for months to years

The authors present the clinical case of a female child aged 6, with no relevant personal or family history, who was admitted in Pediatric Emergency Department (PED) due to edema, erythema and pain on right hand and ankle that started 12 hours earlier. There was no association with trauma, fever or insect bite. Ibuprofen was administered with no effect, and the same results were obtained after oral cardiotherapy and H1 anti-histamines. Intravenous cardiotherapy at 1.5 mg/kg/day was initiated, with clinical improvement in 12 hours, and she was referred to the outpatient clinic. Reviewing history, the patient had suffered several episodes of skin and joint edema in the last 4 months, two of which were associated with mild abdominal pain and diarrhea and had noticed improvement with Ibuprofen. The two episodes with abdominal pain were associated with prior tooth extraction (<12 h before). Laboratory investigation was as follows: negative ANA and anti-dsDNA, CH50 < 13.7 U/mL, C3 89 mg/dL, C4 3.1 mg/dL, C1 inhibitor 62 mg/dL, functional C1 inhibitor 29% (confirmed with 2nd sample). Both parents and siblings had normal levels of C1 inhibitor and functional C1 inhibitor. After the diagnosis, she had two episodes of skin angioedema; she was medicated with tranexamic acid, with good response. Genetic testing is pending.

Discussion: Hereditary angioedema due to C1-inhibitor deficit represents 15-20% of cases. A positive family history is the main warning sign for the diagnosis, but in 20-25% of patients the disease is the result of a de novo mutation. In these cases, it is necessary to have a high suspicion index, because a delay in diagnosis can result in serious consequences. There are limited options for treating children under the age of 12.

TP0823 | Autoinflammatory syndrome with recurrent neutrophil-rich urticarial exanthema, excessively increased inflammatory markers and response to anakinra in a 77 year-old male patient

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Case report: Autoinflammatory diseases (AID) comprise a heterogeneous group of inflammatory disorders characterized by innate immune dysregulation. Many AIDs are associated with genetic defects that cause an uncontrolled secretion of proinflammatory interleukin (IL)-1b. Most AIDs manifest during childhood or early adulthood. Within the group of AIDs, Schnitzler syndrome is an exception, typically starting in the second half of life presenting with urticarial rash, fever, arthralgia and monoclonal gammopathy.

We here present the case of a 77 year-old patient, who developed a recurrent urticarial exanthema at the age of 75. Skin lesions were always accompanied by pronounced leukocytosis, increased levels of C-reactive protein (up to 200 mg/l) and serum amyloid A (up to 100 mg/dl), but no fever arthralgia or other systemic symptoms. A monoclonal gammopathy was not present. Each disease episode lasted for about 10 days, with symptom-free intervals of 3-6 weeks. Elevated inflammatory markers declined to normal levels between disease episodes.

Complete clinical workup included dermatohistopathological examination, documentation of the time course of inflammatory markers, comprehensive search for infectious and neoplastic diseases, echocardiography, gastro-/colonoscopy, FDG PET-CT and next generation sequencing (NGS) panel diagnostics for autoinflammatory diseases.

Multiple skin biopsies of the cutaneous lesions at different timepoints showed a neutrophil-rich inflammatory dermal infiltrate. Thorough investigation of possible infectious or neoplastic causes failed to reveal any underlying disease. NGS panel diagnostics showed no evidence for genetic alterations in the genes ELANE, IL1RN, IL36RN, LPIN2, MEFV, MVK, NLRC4, NLRP12, NLRP3, NOD2, PSMB8, PSTPIP1, TMEM173 and TNFRSF1A. The patient's symptoms did not respond to treatment with antihistamines or dapsone. However, administration of Anakinra 100 mg s.c. resulted in immediate resolution of symptoms and inflammation markers.

Under continued treatment with Anakinra, the patient has remained symptom-free during follow-up for more than 1 year.

Our case indicates that the typical symptom combination of Schnitzler's syndrome may only represent a subset of a larger group of urticaria-like late-onset autoinflammatory syndromes. We recommend that physicians pay attention to the course of inflammatory markers in patients with recurrent non-itching urticaria-like rashes to recognize patients with this kind of disease.

TP0824 | Minor leukocyte subsets in patients with stage Ii pancreatic cancer

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Background: Pancreatic cancer (PC) remains one of the most difficult problems of oncology, associated primarily with unsatisfactory treatment results and extremely poor prognosis. PC in Belarus has an incidence of 8-9 cases per 100 thousand people. This study assesses minor leukocyte subsets in patients with PC.

Method: 15 patients with stage II PC were included in the study (ClinicalTrials.gov ID NCT03114631) before treatment with dendritic cells. The control group (C) comprised 23 healthy volunteers. Minor leukocytes subpopulations, which play an important role in the pathogenesis of oncological diseases, were assayed: myeloid-derived suppressor cells (MDSC): G-MDSC ($lin^-HLA\text{-}DR^-CD11b^+CD15^+$), M-MDSC ($lin^-HLA\text{-}DR^-CD14^+$), regulatory T cells ($CD4^+CD25^{hi}CD127^-CD39^+$), exhausted T cells ($CD8^+CD223^+$, $CD8^+CD366^+$, $CD8^+CD279^+$), as well as $CD4^+$ or $CD8^+$ subsets (Naïve – $CD45RA^+CD45RO^-CD197^+$, TCM – $CD45RA^-CD45RO^+CD197^+$, TEM – $CD45RA^-CD45RO^+CD197^-$, TEMRA – $CD45RA^+CD45RO^{+/-}CD197^-$).

Results: Patients with PC were characterized by increased G-MDSC (C – 0.02%, range 0.01 to 0.05%; PC – 0.12%, range 0.08 to 0.20%; $P = 0.0002$) and M-MDSC (C – 0.32%, range 0.23 to 0.37%; PC – 5.41%, range 2.97 to 8.47%; $P = 0.00003$) counts compared with the control. Lag-3^+ exhausted T-cells were increased in patients with the PC ($P = 0.00005$), while median values of Tim-3^+ and PD-1^+ cells subsets did not differ from the Control. There were also no differences in the Tregs and $CD39^+$ T-regs (C – 1.11%, range 0.97 to 1.28%; PC – 1.01%, range 0.70 to 1.28%; $P = 0.427$) counts between the groups. Both $CD4^+$ and $CD8^+$ T-cell naïve/memory subpopulations exhibited a statistically significant shift towards TEM/TEMRA subsets.

Conclusion: This study demonstrates increased immunosuppressive environment (MDSCs, exhausted T-cells, altered distribution of T-cell naïve/memory subsets) in the patients with the pancreatic cancer compared with control subjects.

TP0825 | The role of cytokine regulation in the progression of obstructive jaundice of malignant origin

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Background: Obstructive jaundice (OJ) of malignant origin is characterized by the appearance of an obstacle to the flow of bile into the duodenum as a result of malignant tumor growth. The severity of the condition and features of progression depend not only on the duration of the OJ itself, but also on the characteristics of the malignant growth. The purpose of this study was to study the characteristics of cytokine regulation in OJ of malignant origin.

Method: 92 patients with OJ due to cancer of the hepatic ducts and 125 healthy individuals were examined. Determination of cytokines (IL-4, IL-2, IL-8, TNF-alpha, Interferon-gamma) in the serum was carried out by enzyme-linked immunosorbent assay using test systems of "Vector-Best", Russia. Statistical data processing was performed using Statistica for Windows 8.0 application packages with determination of the median (Me) and interquartile range (C_{25}-C_{75}). The statistical significance of the differences was determined using the Mann – Whitney rank test $P < 0.05$.

Results: The levels of IL-2, TNF-α, INF-γ and IL-18 were increased in the group of patients with OJ of malignant origin and the IL-4 and IL-10 values were reduced compared to the control group.

Conclusion: An increase in pro-inflammatory and a decrease in anti-inflammatory cytokines was detected in patients with OJ of the malignant genesis; the Th1-pathway of the immune response was observed mainly. The severity of the condition of patients with OJ of a malignant origin before the operation is largely due to hyperbilirubinemia, endotoxicosis, and the development of systemic inflammatory changes.

TP0826 | Features of the functional activity of neutrophils in obstructive jaundice of cholelithiasis

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Background: Obstructive jaundice (OJ) - a clinical condition due to the presence of an obstacle to the flow of bile into the duodenum.

Most often, the syndrome of obstructive jaundice of benign genesis is due to the presence of cholelithiasis. Pronounced changes in the immune system are probably responsible for the progression of the pathological process and the development of complications. The purpose of this study was to study the features of the functional activity of neutrophils (N) in OJ of cholelithiasis.

Method: 84 patients OJ and 125 practically healthy individuals were examined. To study the activity of neutrophilic granulocytes, we used a chemiluminescent analysis of spontaneous and induced neutrophils production of reactive oxygen species. Statistical data processing was performed using Statistica for Windows 8.0 application packages with determination of the median (Me) and interquartile range (C_{25}-C_{75}). The statistical significance of the differences was determined using the Mann – Whitney rank test $P < 0.05$.

Results: In the group of patients with OJ, the area under the spontaneous and induced chemiluminescence curves and the time to reach the maximum of the induced luminescence were increased compared with the control group. In addition, in this group of patients, there was a decrease in the levels of intensity of spontaneous and induced chemiluminescence compared with practically healthy individuals.

Conclusion: The insufficiency of the functional activity of the nonspecific immune system (neutrophil) is due to the effects of the main pathogenetic factors of the development and progression of the OJ: hyperbilirubinemia, acholia, endotoxicosis, development of the systemic inflammatory response.

TP0827 | Peculiarities of TLR9 expression on immunocompetent cells in patients with the reactive arthritis induced by the Epstein-Barr viral infection and the rheumatoid arthritis

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Background: The toll-like receptors play a crucial role in the anti-infective protection of the body. Additionally, the research proves that TLR are actively involved in the development of autoimmune diseases. In recent years one may observe the substantial prevalence of the reactive arthritis (ReA) and the rheumatoid arthritis is referred to the most widely-spread autoimmune diseases. Currently special attention in the development of ReA is paid to the role of viral infection, including the Epstein-Barr virus (EBV). Aim. To conduct the comparative analysis of TLR9 expression on mononuclear cells of the peripheral blood in patients with the rheumatoid and the reactive arthritis with and without EBV infection.

Method: 64 patients have been examined (33 - ReA and 31 - RA). The general laboratory and immunological research has been performed; the serological markers have been determined and the molecular genetic testing has been carried out.

Results: The average age of the patients with the EBV-induced reactive arthritis has been found lower and consisted 26.5 ± 7.4 years with the bigger part of male patients (56.6%), than the average age of the patients with the rheumatoid arthritis 43.2 ± 6.9 years with the bigger part of female patients (76.2%). The inflammatory markers (increased ESR, CRP) were typical for patients with the reactive and the rheumatoid arthritis. The activity of the inflammatory process according to the visual analogue scale and the activity index DAS28 was significantly higher in patients with the rheumatoid arthritis than in patients with the EBV-induced reactive arthritis. The number of TLR9 + CD123 + -monocytes has been defined as significantly ($P < 0.05$) bigger in the blood of patients with the rheumatoid arthritis than in patients with the EBV-induced reactive arthritis and the number of TLR9 + CD123 + -lymphocytes has turned out to be bigger only in the active phase of the EBV-infection in patients with RA.

Conclusion: There exists the possibility of additional mechanisms which at EBV-infection restrain the development of autoimmune reactions till certain moment and TLR9 depending upon the genetic peculiarities and the microenvironment can activate or suppress the inflammation, including the one of the autoimmune genesis. Application of the antiviral drugs can hold back the intensification of the inflammatory process, including the one of the autoimmune origin.

TP0828 | Refractory leukocytoclastic vasculitis—Case report

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Case report: Leukocytoclastic vasculitis is a small vessel hypersensitivity vasculitis that can be triggered by drugs, infections, autoimmune diseases and malignancies. It usually manifests as a palpable purpuric rash mainly affecting the lower limbs, with or without visceral involvement.

We present the case of a 43 year old female patient suffering from histologically confirmed leukocytoclastic vasculitis of 6 year duration. Extensive screening for underlying causes has been repeatedly performed since the onset of the disease. Drug induced vasculitis, connective tissue disorders, and neoplasia have been excluded. Screening for infectious diseases only revealed recurrent lower urinary tract infection for which the patient has been thoroughly evaluated and treated by an urologist. Significant clinical improvement was initially achieved using dapsone and colchicine, but after a few months this combined treatment failed to maintain disease control despite dosage increase. The patient did not respond to several other treatments such as systemic corticosteroids associated with immunosuppressive agents, hydroxicloroquine or methotrexate, leaving few therapeutic alternatives.

We wish to discuss the possible etiologic factors for leukocytoclastic vasculitis in our patient and the therapeutic options in such refractory cases, with emphasis on biologic treatment.

TP0829 | Functional characteristics of B2 lymphocytes with varying degrees of activity of the seropositive variant of the course of articular rheumatoid arthritis

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Background: One of the components of the immune system involved in the pathogenesis of RA are B-lymphocytes, which are characterized by polyclonal activation. However, their population is not homogeneous, and the role of each of the phenotypes (B1,B2) depending on the degree of activity of autoimmune process discutable. Goal is to study the functional features of B2 lymphocytes, depending on the degree of activity in the seropositive variant of the course of articular RA

Method: A total of 51 patients were examined in the acute stage with a seropositive variant of articular RA, of which 26 people had II degree of activity, and 25 patients III. The control group consisted of 20 healthy donors. Immunological research methods included determination of antigens of

B2 - lymphocytes: CD19+, CD23+, CD25+, CD40+, CD86+, CD27+, CD19+CD95+, CD19+An + flow cytometry

Results: In a comparative analysis of B2 cells in patients with seropositive RA, depending on the degree of activity, a statistically significant increase in the relative number of naive B2 lymphocytes (CD19 + CD27-) was detected in degree III activity (8.13 ± 0.85%, 11, 3 ± 0.97%) than with II. Whereas, the number of B2 cells of mature (CD19 + CD5-) and memory (CD19 + CD27 +) did not depend on the degree of activity. As the disease progressed, no statistically significant changes in the expression of markers of early activation (CD19 + CD23 + , CD19 + CD25 +) on B2 lymphocytes and their readiness for apoptosis (CD19 + CD95 + , CD19 + An +) were not detected. At the III degree of activity compared to II, a statistically significant increase in the expression of the core-receptor molecule CD40 (9.71 ± 0.93%, 13.2 ± 1.23%) was detected on CD19 - lymphocytes, while expression of the ligand to CD40 (CD40L) on T-helper cells and the CD86 + molecule on B2 cells did not significantly change with the progression of RA

Conclusion: Thus, with an increase in the degree of activity of the inflammatory process in seropositive RA, changes in the phenotype of B2 cells are revealed, which are characterized by an increase in the expression of membrane markers: CD5 + CD40-, which can be used as laboratory markers of the activity of the autoimmune process.

TP0833 | Vitamin D deficiency and treg cell insufficiency in patients with secondary systemic vasculitis

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Background: In several autoimmune diseases compromised regulatory T cell (Treg, CD4 + /CD25 +) function is critically involved in the disease process. *In vitro*, biologically active metabolites of vitamin D have been shown to promote Treg development. A potential *in vivo* correlation between vitamin D status and Treg function in a relapsing course of secondary systemic vasculitis (SSV) patients was assessed.

Method: Plasma 25(OH)D_3 levels were assessed in 96 patients with secondary systemic vasculitis. Patients were divided into two subgroups: 49 patients with virus induced secondary vasculitis and PCR virus DNA replication; and 47 patients with secondary systemic vasculitis without PCR DNA virus replication. Autoantibody profiles (anti-U1-ribonucleoprotein, anti-SSA, anti-SSB, anti-Jo1, anti-Scl70, anti-double-stranded DNA, anti-centromere (Polycheck-tests, Biocheck, Germany) and clinical symptoms of the patients were assessed.

Results: Plasma levels of 25(OH)D_3 in patients with SSV were significantly lower compared with controls in both groups (SSV without virus replication: 22.2 ± 8.4 ng/mL versus control: 43.7 ± 9.8 ng/mL, $P = 0.01$; SSV with virus replication: 12.6 ± 6.3 ng/mL versus control: 43.7 ± 9.8 ng/mL, $P = 0.0001$). The presence of active dermatological symptoms (photosensitivity, peripheral rash, erythroderma, heliotrope rash, Gottron's papules) was associated with low levels of vitamin D3. Patients who progressed into chronic fatigue syndrome and recurrent *herpetic gingivostomatitis* with SSV had lower vitamin D levels and Treg lymphocytes (CD4 + / CD25 +) than those who remained in the SSV stage without other immune dysfunction syndromes (vitamin D levels: complicated SVV: 12.6 ± 6.3 ng/mL versus not complicated SSV: 22.2 ± 8.4 ng/mL, $P = 0.01$).

Conclusion: These results suggest that vitamin D deficiency and decreased function and level of Treg cells in SSV patients may play a role in the subsequent progression into complicated and therapy resistant SSV with future development of chronic fatigue syndrome, and immunodeficiency.

TP0834 | PFAPA syndrome in Slovakia

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Background: PFAPA syndrome (the syndrome of Periodic Fever, Aphthous stomatitis, Pharyngitis and cervical Adenitis) is idiopathic autoinflammatory condition. It is the most common periodic fever syndrome in childhood. The current pharmacological treatment includes corticosteroids, which are effective in the management of fever episodes. There are many options for the prophylaxis of febrile episodes (e.g. *anakinra*, *ketofifen*, *colchicine*, oral probiotics); however, their efficacy is different. Tonsillectomy is an option for selected patients with frequent episodes. PFAPA syndrome is usually benign condition which spontaneously resolves till adulthood.

Method: We present our group of patients with PFAPA syndrome. All of them were diagnosed according to valid clinical criteria in our Centre for periodic fever syndromes in Martin, Slovakia.

Results: Till this time we have 144 patients with this diagnosis, 74 boys (51.4%) and 70 girls (48.6%), at the age of 4.01 ± 2.78 years. The mean age of onset of symptoms is 2.26 ± 1.92 years. Positive family anamnesis for PFAPA is in 21.36% of patients. The interesting fact is that 47.57% has positive allergic anamnesis (33.9% inhaled allergies; 18.45% food allergies; 10, 68% drug allergy). About 50% of patients have complete clinical picture (fever, aphthous stomatitis, cervical adenitis and pharyngitis), 100% of patients have fever during attacks; pharyngitis and cervical adenitis is present in 96% of patients during attacks, 50% of patients have aphthous stomatitis. All of our patients have elevation of inflammatory parameters (CRP, SAA, IL-6) during attacks. All of the patients are treated with prednisone during episodes with excellent clinical response (mean dose of prednisone is 1.3 mg/kg/dose). For the prophylaxis of febrile episode we use *ketotifen* with positive therapeutic effect in 63% of patients. Oral probiotics (*Streptococcus salivarius K12*) were used in 22 patients with recurrent aphthous stomatitis with good outcome in 5 of them. Tonsillectomy was indicated in 14% of patients with excellent clinical response.

Conclusion: PFAPA syndrome is the most common periodic fever syndrome in childhood. It has a good prognosis but can affect patient's quality of life in the first years of life. This one of the first reports from Slovakia about this interesting group of patients.

TP0835 | Neutrophilic urticarial dermatosis (NUD) comorbidity of/a manifestation of drug-induced lupus?

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Case report: Introduction: Neutrophilic urticarial dermatosis (NUD) is a condition that is underdiagnosed. NUD has been described in patients with cryopyrin-associated periodic syndromes, Schnitzler syndrome, adult-onset Still's disease, systemic lupus erythematosus (SLE), malignancy, and autoimmune thyroiditis. NUD clinically resembles classic urticaria but when preceded by SLE is frequently interpreted as a lupus flare. Drug-induced lupus is a clinical entity, with features similar to SLE. Currently, there are no reports of NUD as a comorbidity of/a manifestation of drug-induced lupus.

Case presentation: A 64-year-old female patient addressed our clinic for a pale papular, moderately itchy rash reminding of urticarial lesions and arthralgia. The onset of symptoms was 6 weeks prior to the presentation and the response to antihistamines was poor. Potential significant associated pathology such as autoimmune thyroiditis, Hepatitis C virus infection, arterial hypertension and pulmonary sarcoidosis for which the patient was receiving treatment with bisoprolol and candesartan was present.

Results: Due to the particular history of the patient a skin biopsy which showed an intense neutrophilic infiltrate in the dermis with leukocytoclasia without significant edema, neutrophilic epitheliotropism or fibrinoid necrosis of vessel walls has been performed at the presentation. Immunofluorescence demonstrated complement deposition although rather unspecific making an SLE or vasculitis diagnosis less probable. Extensive paraclinical investigations included auto-antibody screening which indicated positive Anti-dsDNA (37.0 UI/mL) and anti-Ro (15.9 u/mL) antibodies. A NUD diagnosis was made and treatment with dapsone was decided. Unfortunately, the patient developed severe epigastralgia and melena and dapsone was stopped. The patient was put again on treatment with antihistamines (quadruple dose) which did not offer control of the symptomatology. The diagnostic was rethought and the possibility of a NUD associated drug-induced SLE was considered. Interestingly withdrawal of bisoprolol (possible culprit) led to complete disappearance of the lesion after one week without recurrence.

Conclusions: We present the case of NUD, with positive serology for SLE which included antibodies specific for drug-induced disease and possible culprit drug exposure (bisoprolol) in which after withdrawal of medication the lesions have completely cleared off.

TP0836 | Etiology and prevalence of Stevens-Johnson syndrome in Ukraine

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Background: Stevens-Johnson syndrome (SJS) is a commonly observed severe systemic allergic delayed-type reaction, characterized by the expressed intoxication syndrome, lesions of skin and mucous membranes.

Method: During recent 15 years we observed 78 children with SJS. Children under the age of 1 year — 5.13%, 1-3 years — 20.51%; 3-6 years — 24.36%; 6-12 years — 38.46%; 12-18 years — 11.53%. 47 (60.26%) of patients were boys and 31 (39.74%) - girls. Family history of allergies had only 13 (16.67%) children. Etiological factors were the following: respiratory infection — 20 (25.64%), medicines — 45 (57.69%), reason undefined — 13 (16.67%). The most common cause of SJS among drugs were multivitamins — 24 (53.33%); biosupplements — 4 (8.89%); antibiotics — 5 (11.11%); other drugs — 12 (26.67%). Penicillin antibiotics have not caused SJS during the entire observation period.

Results: Infusion therapy was performed according to Holiday-Segar method. Antibiotics were not used in most of the patients (54). Systemic therapy with oral corticosteroids (OCS), mainly prednisolone, was performed in most of the cases (53 cases; 70.67%). Daily doses of hormones were: 1-1.5 mg/kg in 41 patients (77.36%); 2-3 mg/kg — 8 (15.09%); 10 mg/kg — 4 (7.55%). Patients on the maximum OCS dose developed severe complications (osteomyelitis, pneumonia and keratitis). During these years 11 patients received normal human immunoglobulin 0.5-1 g/kg QD for 3-4 following days.

Complications during the recovery period were the following: pneumonia — 2; osteomyelitis — 1, thrombopenia — 1, local skin atrophy — 1. These complications developed during the 1 to 3 months after the discharge from the hospital. 3 patients with SJS developed asthma and 3 developed keratitis during the year after recovery. Patient who received human immunoglobulin did not develop any complications. The period of observation over the reconvalescent patients was 6-10 years. There were no repeat cases of drug allergies during this period.

Conclusion: Intravenous administration of normal human immunoglobulin inhibits the progression of skin and mucous membranes lesions. Its use has a protective impact and decrease the risk of complications in this group of patients.

TP0837 | Immunological parameters in psoriasis and psoriatic arthritis patients in Eastern Siberia of Russia

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Background: Psoriasis (PS) is a chronic inflammatory and immunopathological mediated skin disease characterized by proliferation of keratinocytes, excessive angiogenesis and immunological dysfunctions. Psoriatic arthritis (PsA) is one of the severe and disabling clinical forms of psoriasis. Despite major breakthroughs in research devoted to PS and PsA pathogenesis there are no clear data about the features of cellular and humoral immunity in psoriatic disease progression. Aim. To study the concentration of pro-inflammatory and anti-inflammatory cytokines, indicators of cellular and humoral immunity and conduct a comparative analysis in psoriasis and psoriatic arthritis patients.

Method: We formed 3 cohorts: 1 — PS (n = 67), 2 — PsA (n = 60), 3 — control group healthy blood donors (n = 103). All individuals were Russians from Krasnoyarsk Territory (Eastern Siberia). Population and subpopulation of blood lymphocytes was evaluated by flow-cytometry using monoclonal antibodies to CD3, CD4, CD8, CD16, CD19. Phagocytic activity of peripheral blood neutrophils was assessed microscopically by uptake of latex particles. Concentrations of immunoglobulins (IgA, IgM, IgG), circulating immune complexes -C1q and -C3d (CIC-C1q and CIC-C3d), cytokines (IL-4, IL-6, IL-10, TNF-α) in serum were measured by ELISA.

Results: We identified that PS and PsA characterized by statistically significant increased levels of $CD16^+$ lymphocytes, phagocytic neutrophils, serum concentrations of IL-6 and CIC-C1q and decreased phagocytic number, serum concentrations of IgA, IgM, IgG, IL-10 compared to control. We revealed that in psoriasis compared to control group an increased concentration of $CD8^+$ lymphocytes in peripheral blood was noted, while in psoriatic arthritis — increased serum concentrations of TNF-α, IL-4 and CIC-C3d. Psoriatic arthritis characterized by increased serum concentrations of TNF-α, IL-4 and CIC-C3d compared to psoriasis.

Conclusion: We identified features in immunological parameters in PS and PsA which indicate the presence of both common changes compared to the control and intergroup differences considered as markers of psoriatic disease progression.

TP0838 | An unexpected malignancy in children with ataxia telangiectasis: Intracerebellar hemangiopericytoma

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Case report: Introduction: Ataxia Telangiectasia (A-T) is characterized by progressive cerebellar degeneration, telangiectasia, immune deficiency, recurrent sinopulmonary infections, radiation sensitivity, premature aging, and predisposition to malignancy, particularly lymphoid origin. These patients have high cancer incidence (life-long risk of approximately 25%), while lymphomas and leukemias are seen in A-T patients under 20 years of age, while there are several solid tumors in adults, both lymphoid tumors and breast, liver, stomach and esophageal carcinomas. Particularly in pre-leukemic T and B lymphocyte clones chromosome 14q11, 14q32, 7q35, 7p14, 2p11 and 22q11 fractures and chromosome rearrangements are seen. Hemangiopericytoma is a mesenchymal tumor of fibroblast origin which develops as dural or extradural and it is aggressive. The descriptive molecular change in this tumor is the fusion between different exons of NAB2-STAT6 (detected by WES). We report a 7-year-old girl with A-T who developed intracranial hemangiopericytoma.

Case: A two-year-old female child was diagnosed with ataxia by his family and was diagnosed with AT due to cerebellar ataxia, bilateral fetal, alpha-fetoprotein (AFP) elevation, and hyper Ig M syndrome at the age of 4.5 years. No mutation analysis was performed. She was followed-up with the diagnosis of ataxia telangiectasia. Monthly IVIG and prophylactic bactrim treatments were started. In the second year of follow-up, the patient developed in the left eye with gliding, gushing vomiting, headache and evaluated by emergency cranial MRI. She was operated because of herniation and signs of kibas. The mass was totally resected. In the pathological evaluation, solitary fibrous tumor/hemangiopericytoma was reported as > 5 mitosis/10 hpf, grade 3 (WHO, 2016). The patient received only cranial radiotherapy. Because of the tumor size and grade 3, our patient has a high risk of recurrence.

Conclusion: Our case is interesting because, as far as we know, the patient presented with a tumor that we have never encountered in PubMed as a solid tumor of A-T in pediatric patients, so far.

TP0839 | Interleukin-21 receptor (IL-21R) deficiency in a patient with difficult asthmatic and multiple food allergy and CVID-like conditions following early childhood

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Case report: Introduction: Interleukin -21 (IL-21) is a cytokine which function through IL-21 Receptor (IL-21R) and produced by helper T cells in the lymph nodes' germinal centers and allowing B lymphocyte differentiation during antibody response. However, Tfh cells which carry CXCR5, has recently been found to function not only in follicles but also in blood and tissues, especially in tonsils, as subgroups of NKT cells, gamma-delta T cells and Tregs, all of which function through IL-21. IL-21-producing Treg cells in tonsils have been shown to inhibit allergen degranulation of the effector cell, suppress Th2 cytokines, and thereby suppress the sensitization and effector phase of the allergic reaction.

Case: 19-year-old patient born from first-degree consanguineous marriage, presented to our hospital. Since her infancy with difficult asthma, frequent anaphylaxis caused by multiple food allergies, frequent urticaria or urticaria-angioedema attacks; allergic rhinitis, frequent and severe URTI and sinobronchial infections (no opportunistic infections, Candida, HSV, HPV, EV, MC, Tbc, chronic diarrhea,) Her serum total IgE level increased to 30.000 (HIES scoring: 10 that is not compatible with HIES). Immunological screening tests were performed. At the age of 12, the decrease in immunoglobulin levels were detected and put on prophylaxis with TMP-SMX (IgG: 500 mg/dl; N for age between mg/dl). Lymphocyte flow cytometric analysis revealed a slight B cell deficiency (11%, Absolute: 289/mL, $IgD^{-}CD27^{+}$ Memory B cells 6%); CD4/CD8 ratio was reversed (0.7). She was diagnosed as CVID. She begun to have nausea and urticaria when she ate chicken and meat in November 2016, Omalizumab no significant improvement

In order to exclude Primary Immunodeficiency, it was planned to investigate the PID genes with Next Generation Sequencing (NGS). The most likely candidate variant was the homozygous IL-21R mutation (high CADD score 35) and was accepted as the gene that caused the disease. Repeatedly confirmed (missense mutation leading to premature stop codon pS474 *, Kaan Boztug Lab, Vienna Austria)

Discussion: We believe that the molecular defect (IL-21R defect) found in our patient with severe asthma symptoms despite various drug therapies and infections suggesting immunodeficiency may explain the clinic although there is no IBD yet.

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TP0840 | Clinical value of basophile activation test in cashew nut allergy

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Background: The clinical value of basophile activation test (BAT) in the diagnostics of food allergy is still unclear. This study aimed to investigate BAT as a diagnostic tool in IgE mediated cashew nut allergy. We also assessed serum baseline tryptase levels as well as changes in tryptase levels after allergic reaction.

Method: We performed between January 2015 and December 2018 fifty-nine open cashew nut challenges for 1-13-year-olds with cashew nut sensitization and previous symptoms or no known exposure to cashew nut. The starting dose was 5 mg, followed by increasing doses of 25, 50, 100 and 500 mg cashew protein. The blood samples were drawn and skin prick tests were performed to all the patients. Total blood count, serum total IgE and specific IgE against birch, cashew nut, hazelnut, peanut, walnut, Ara h 1,2,3,6,8,9, Cor a 1,8,9,14, Ana o 3, Jug r 1 and Ber e 1 were measured. On the challenge day basophile activation test for cashew nut was done to all patients. We assessed serum baseline tryptase levels before the challenge and in the positive challenges also 60, 120 and (240) minutes after clinically significant symptoms occurred. In the negative challenges one additional tryptase measurement was performed just before patient was discharged. All the challenges were done by the same pediatrician. The positive challenge reactions were determined based on Practall guidelines and the severity of reactions was assessed.

Results: Median cashew nut IgE was 0.67 (range 0.00-55.30) and median Ana o 3 IgE was 0.41 (0.00-52.70) kU/l. Thirty-five (59%) of the challenges were positive. Eleven (19%) patients had a mild reaction and 23 (40%) a moderate to severe reaction. Gastrointestinal symptoms (82%) were most common, 41% had skin and 44% had respiratory symptoms. One patient had cardiovascular symptoms (3%). Twenty-one (60%) of challenge positive patients received epinephrine. Cashew nut-BAT with 10% cut-off was positive in 79% of the moderate to severe reaction group, 50% in the mild reaction group and in 12% in those with no clinical reaction.

Conclusion: Cashew nut-BAT may be a promising new tool in predicting the risk of allergic reaction in cashew nut sensitized patients. More studies with bigger sample size are needed.

TP0841 | Differential IgE binding to freshwater and seawater fishes in a chinese population of fish allergic subjects

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Background: Diagnosis of fish allergy is often based on a few representative seawater fishes. We sought to compare the IgE reactivity of freshwater and seawater fishes in a Chinese population where freshwater fishes are part of traditional Chinese diet.

Method: 98 subjects with physician-diagnosed immediate-type allergic reactions to fish were recruited from five hospitals in Hong Kong. To compare the IgE reactivity of freshwater and seawater fishes, blood samples were collected from the subjects and their IgE reactivities against cod, tuna, salmon, catfish and tilapia were measured by ImmunoCAP test. To compare the IgE reactivity at a component level, IgE reactivities against the major fish allergen parvalbumin from cod (rGad c 1) and common carp (rCyp c 1) were also measured by ImmunoCAP.

Results: All subjects had 0.35 kU_A/L IgE against at least one of the five fishes tested by ImmunoCAP. Twenty subjects (20.4%) were sensitized to catfish and/or tilapia only with no IgE reactivity detected against any of the seawater fishes. In contrast, only one subject was sensitized to tuna and salmon without detectable IgE against freshwater fishes. Two subjects were monosensitized to tilapia, while two other subjects were monosensitized to salmon or tuna. Among the seawater fishes, IgE reactivity is significantly lower against tuna (median: 0.58 kU_A/L; IQR: 0.21-1.55 kU_A/L) than to cod (median: 1.14 kU_A/L; IQR: 0.34-3.20 kU_A/L) or salmon (median: 0.87 kU_A/L; IQR: 0.24-3.10 kU_A/L), while the two freshwater fishes catfish (median: 4.19 kU_A/L; IQR: 1.20 — 13.3 kU_A/L) and tilapia (median: 4.69 kU_A/L; IQR: 1.29 — 16.23 kU_A/L) had a stronger IgE reactivity than all of the above seawater fishes. Most subjects were IgE reactive to tilapia (n = 95, 96.9%) while least subjects were IgE reactive to tuna (n = 59, 60.2%). For the fish components, IgE reactivity against the common carp parvalbumin rCyp c 1 (median: 5.80 kU_A/L; IQR: 1.32 — 16.1 kU_A/L) was significantly higher than the cod parvalbumin rGad c 1 (median: 3.67 kU_A/L; IQR: 0.68 — 10.4 kU_A/L).

Conclusion: IgE reactivity against freshwater fishes is significantly stronger than seawater fishes in our population at both extract and component levels. Freshwater fishes should be taken into consideration for better diagnosis and clinical management of fish allergy.

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TP0842 | Molecular diagnosis could rule out hypersensitivity in patients with suggestive history of shrimp allergy

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Background: Immediate hypersensitivity reactions to shrimps represent the major proportion of allergy to sea food. Recombinant protein *Penaeus aztecus* (rPen a 1), has been proven and commercialized to help in the diagnostic process. The aim of this report is to describe the predictive value of rPen a 1 in patients with suggestive history of immediate hypersensitivity to shrimps.

Method: Patients with history of immediate reaction to shrimps and positive skin prick test and/or specific IgE to shrimps, were prospectively included. In each one of them, the specific IgE against the recombinant allergen r Pen a1 (immunoCAP technique) was tested. An oral challenge with shrimps was carried out in those with undetectable results (< a 0.1 UI/L).

Results: Nine patients (six women and three men), met the inclusion criteria. The median age was 29 years (9 to 62). The serum determination of rPen a 1 was undetectable in all of them. All nine patients accepted the realization of an open oral challenge with shrimp, and all of them tolerated it. Informed consent was obtained before the challenge.

Conclusion: The diagnostic approach of crustacean allergy should include the determination of some major allergens by recombinant allergen technique. It seems to be that the absence of specific IgE against rPen a 1, predicts the negativity in the oral challenge with shrimps, even in patients with suggestive history and positive skin prick test and/or positive specific IgE to the whole food. Given the importance of this finding, the persistence of tolerance state must be monitored in time.

TP0843 | Self-reported food allergic symptom and Results of IgE sensitization in children

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Background: The diagnosis of food allergy need to be confirmed by oral food challenge (OFC). However, specific IgE (sIgE) sensitization results analyzed by serologic or skin tests are also help to predict the OFC outcome and determine the test items. Unfortunately, there is a limit to the number of antigens that can be evaluated at one time. The purpose of this study was to analyze possibility of detection of specific IgE antibody to the food using clues in self-report food allergic symptoms.

Method: From May 2011 to December 2013, medical records of patients aged 3 years or younger who visited at the Department of Pediatrics in Ajou University Hospital were collected retrospectively. Egg white-, cow's milk-. walnut-, and soybean-sIgE sensitization (>0.35 kU/L, ImmunoCAP, Thermo Fisher Scientific Inc., Uppsala, Sweden) and its related clinical histories were evaluated. Classified according to symptoms; If the reaction by direct-isolated intake is 1) class 1: anaphylaxis or hive -if the repeated exposure results were not consistent, classified as class 2-, 2) class 2: itch without hive, vomit, and diarrhea 3) class 3: asymptomatic. However, class 1, in which the symptom onset time was recorded as 'next day', was again classified as class 2. In addition, all cases that are not direct-isolated intake were considered to be vague and class 1 classified as class 2 except anaphylaxis due to skin exposure, which still regarded as class 1. Receiver operating characteristics (ROC) were analyzed.

Results: A total of 337 cases (116 egg white, 182 cow's milk, 17 walnuts, 22 soybeans) were collected. The most frequent self-reported reactions was hives and cow's milk was the main cause of vomiting and diarrhea. There was more nonspecific itching by milk and soybean than egg white and walnut. The AUC of class 1 for cow's milk was 0.790 and the accuracy was 78.0%. Accuracy was lower when considering class 2 together in cow's milk. However, the AUC of class 1 together with 2 for egg white was better than class 1, 0.750 and the accuracy rate was 77.6%. The AUC of class 1 for walnut was 0.775 and it of soybean was 0.662.

Conclusion: In this study, sIgE sensitization to the foods could be predicted by the combination of exposure and self-reported related symptoms in children under 3 years of age. Additional research is under way to predict the outcome of OFC.

TP0844 | Tolerance to baked milk in children with cow's milk allergy

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Background: Cow's milk allergy (CMA) is the most common childhood food allergy. Oral food challenge is still the gold standard test for diagnosis. A subset of milk allergic individuals can eat baked milk without allergic symptoms. Through the identification of the patients that can tolerate baked milk, it is possible to improve quality of life for those who have cow′s milk allergy, being able to be set free in its diet products with baked milk.

Method: Patients with CMA were submitted to oral challenge with baked milk, from January 2017 to December 2018 in the Pediatric Allergy and Immunology Department of Trakya University Hospital, Turkey. A retrospective chart review was performed. The tested product was a muffin that contained 1.3 g milk protein and was baked at 350° F in an oven for 30 minutes. The challenge was made under physician supervision and at the first sign of allergy reaction

it was discontinued, and the patient received the proper medical assistance.

Results: Sixteen children (median age, 8 months; range, 4-25 months) underwent heated milk challenges. Skin prick test to cow milk extract was positive 8/14(57%) of patients and specific IgE to cow milk was positive 7/11 (64%) of patients. Fourteen (87%) subjects tolerated extensively heated milk only, 2 reacted to heated milk.

Conclusion: The majority (87%) of children with milk allergy tolerate heated milk. Products prepared with baked-milk may be a good alternative food in daily routine of the majority of children with CMA.

TP0845 | Severity of the presentation of LTP allergy in patients with respiratory symptoms

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Background: Allergy to airborne and food proteins represents a major health problem in Western countries. Lipid transfer proteins (LTPs) are important allergens, and represent a major cause of systemic food allergic reactions in the Mediterranean area(1-3). We have studied the frequency of respiratory symptoms and anaphylaxis in Pru p 3-sensitized patients in a sample at the Alicante General University Hospital (Spain).

Method: Respiratory symptoms were evaluated by a standardized questionnaire in patients sensitized to LTP. Having a papule greater than or equal to 3 mm in skin tests and/or specific immunoglobulin E (IgE) to Pru p 3 quantified by ImmunoCAP ISAC® greater than or equal to 0.3 ISU was considered sensitization to Pru p 3 and those sensitized with clinical symptoms after being exposed to this protein were considered allergic.

Results: In total 403 over 438 sensitized patients, were allergic to Pru p 3. Of these, 161 (36.7%) had anaphylaxis, with a mean age of 34.3 (±11.55) and 43.5% males. Besides, 118 (73.3%), presented rhinitis 31.7% asthma and 23.6% both. Of the 277 (63.2%) Pru p 3 sensitized patients without anaphylaxis, 55.2% had clinical symptoms after being exposed to this protein (such as oral allergy syndrome and/or angioedema and/or urticaria), with a mean age of 32.3% (±10.85) and 41.3% males. Of these, 74% had rhinitis, 30.6% asthma, and 22.3% both diseases.

Conclusion: Allergic respiratory symptoms (allergic rhinitis, asthma or both) are present in the same way in patients presenting food allergy induced by LTP independently of the severity of reaction.

TP0846 | Optimization and merging of food product data and food composition databases for medical use

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Background: The number of dietary apps for iOS and Android is significantly increasing in the relevant app stores. An urgent problem of most nutrition and diary apps is the limited quality and quantity of available food data. In Europe, digital data on food products is not available via one single data source. It but will be collected and distributed by various non-commercial and commercial organizations. Hence, developers of dietary apps have to deal with individually maintained databases, which leads often to quality deficiencies and inconsistencies. Especially when product data are collected by crowd sourcing approaches or volunteer communities, a poor data quality cannot be recognized easily, which limits promised values of app for end users and health professionals.

Method: Within the DiDiER project (funded by German Federal Ministry of Education and Research), a dedicated "Food-Information-Service" (FIS) has been developed. FIS is designed to provide data for nutrition or diary apps, and contains currently data of about 38 000 food items. To detect inconsistent datasets, computer-aided analysis methods are used to evaluate product data from various sources. Comparison and merging of product data and food composition databases help to indicate accurate ingredient information and support the complement of missing nutritional values. In addition, data profiling and cleansing methods are used to remove duplicates or to amend incomplete items. Hence, inconsistencies in the FIS databases are detected and corrected in a semi-automatic approach.

Results: When evaluating optimized data sets, special functions are used to quantify the quality of completeness and consistency of data sets. The comparison of a sample of 1000 optimized records with the same data before optimization shows that the completeness of data attributes has increased from 79 percent to 84 percent in the worst case and from 62 percent to 100 percent in the best case. The consistency of the attributes has increased from 83 percent to 93 percent in the worst case and from 74 percent to 97 percent in the best case.

Conclusion: Quality measurement shows that our method is able to increase the quality of food related data records. By increasing the number of connected databases and processed datasets, the probability to detect incorrect data sets will further increase. In the next step of the project, food data will be optimized in relation to additional quality criteria such as timeliness and believability.

TP0847 | Sesame allergy—To challenge or not to challenge that is the question

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Background: Sesame is the third most common food allergen in Israel, and a cause of fatal allergic reactions. According to current literature sesame allergy is unlikely to resolve, hence allergen avoidance is the prime and only management recommended. Diagnosis of food allergy requires the performance of allergy tests, including a food challenge. Sesame challenge is frequently not performed because this allergy is considered persistent and challenges withhold high-risk of anaphylaxis. In this study we describe the results of sesame allergy evaluation in a tertiary center.

Method: Children with a history of an immediate reaction to sesame were included in this study. All children underwent skin prick test (SPT) and a gradual open food challenge (OFC) with sesame (as natural sesame paste) regardless of SPT results. Oral food challenge was defined as successful OFC if the child could eat sesame at the

Sesame food challenge			Successful	Failed	*P*
Number of children			28 (62%)	17 (38%)	
Male/Female			18/10	8/9	0.266799
Food allergy	Food allergy		15	12	0.268792
	Milk		5	1	0.26198
	Eggs		5	4	0.653606
	Peanut		8	3	0.41992
	Fish		1	4	0.039629
	Soy		2	0	0.269841
	Hazelnut		2	4	0.122306
	Pecan		1	1	0.722808
	Walnut		1	4	0.039629
	Pistachio		1	3	0.112601
	Cashew		1	1	0.722808
	Almond		0	2	0.065681
	Nuts		4	8	0.015347
Atopy	Atopic dermatitis		10	10	0.136424
	Asthma		6	4	0.873079
	Allergic rhinitis		2	3	0.287542
Family	Food allergy		5	3	0.442196
	Atopy		1	0	0.986143
Average age at first allergic reaction (month)			10.93	12	0.818654
Type of reaction	Skin		28	17	
	Respiratory		6	6	0.318825
	Gastrointestinal		1	1	0.722808
	Anaphylaxis		6	5	0.556294
SPT (average)	Commercial	Wheal	5.4	6	0.851465
		flare	9.09	12.6	0.443069
	Natural sesame paste	Wheal	3.95	13.2	0.000494336
		flare	7.82	24.6	6.00382E-05
Sesame specific IgE (average)			1.2	2.09	0.369559
Accidental exposures	Accidental exposures		10	4	0.403516
	Number of accidental exposures		2.9	0.765	0.177446
	Time from last accidental exposure (month)		5.9	67.17	0.327458
Sesame food challenge	Age (month)		55.8	67.2	0.491958
	Sesame protein eaten at the food challenge		10.6	2.112	0.004698392

amount of at least 3 gr and up, with no allergic response, and failed OFC if allergic reaction occurred during the challenge.

Results: A cohort of 45 children with sesame allergy, 19(42%) girls and 26(58%) boys, between the ages of 14 months — 17 years of age, were evaluated. Of which 17(38%) exhibited sesame allergy following challenges while 28(62%) were sesame tolerant. Sesame allergy was associated with concomitant allergy to nuts ($P = 0.015347$), specifically walnut ($P = 0.039629$), fish ($P = 0.039629$) as well as the size of SPT to natural sesame paste ($P = 0.000494336$) but not to commercial reagent. Notably time from last accidental exposure was more than 2 times longer in tolerant compare to allergic children (5.89 month vs 2.23 month respectively), although this did not reach statistical significance.

Conclusion: Open food challenge, although of high risk, is essential for the diagnosis of sesame allergy. In the current study, unlike the common belief, 62% of children suspected to be allergic to sesame could tolerate sesame. Several markers were related to persistent sesame allergy including concomitant sensitization to nut and fish as well as higher skin response to natural sesame paste.

TP0848 | Seeking oleosins

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Background: Recent publications have described oil body-associated allergens called oleosins, that are recognized by IgE antibodies from sensitized patients. They can cause symptoms ranging from mild oral allergy syndrome to severe reactions such as anaphylaxis. Sesame seeds, olives and nuts are the foods most commonly involved. As they are oil body fractions, these sensitizations could be misdiagnosed using conventional allergenic extracts. An Alternative diagnostic with extracts preserving the oil body fraction in each case, could be required. Our objective was to detect sensitization to oil body fractions in patients with symptoms clearly suggestive of food allergy to nuts in which allergic sensitization could not be demonstrated by conventional extracts.

Method: Four patients with symptoms ranging from oral allergy syndrome, to angioedema, urticaria and anaphylaxis in relation to the intake of nuts (peanut, pistachio, cashew, walnut, peanut, almond) were selected. We performed allergological study: prick test with suspect foods, specific IgE and finally immunoblotting to detect the presence of IgE-binding bands, in relation to water soluble and lipid-soluble fractions for almond, cashew, peanut, walnut and pistachio.

Results: In all cases, skin test and specific IgE to implicated foods were negative but western blot revealed IgE binding bands compatible with oil body-associated allergens to peanut and almond in three of the four cases. In one of the cases no fixation of bands was observed for any type of fraction (lipid-soluble or water-soluble).

Conclusion: We present four patients with suspected allergy to nuts with clinical manifestation suggestive of IgE-mediated with negative conventional tests (prick test and specific IgE). In three of the four cases, sensitization to lipid-soluble fractions of peanut and almond was observed through immunoblotting. Although it is a short series of patients, the fact of demonstrating such sensitization, indicates that probably many of the negative tests obtained when studying allergy to nuts are false negatives. It is necessary to go further in the study of these patients, using viable techniques in the usual clinical practice since the immunoblotting is not useful in this aspect. A good option would be to systematically perform prick skin tests with preserving lipid fraction prepared extracts of each food.

TP0849 | Peanut flour protein with defined allergen content for use as reference standard

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Background: Allergen measurements are widely used for determination of the potency of therapeutic allergenic products, environmental exposure assessments, and for validation of IgE molecular diagnostics. However, few standardized allergen reference materials have been developed. The aim was to produce a standardized peanut flour protein with defined allergen content that could serve as a reference standard for peanut diagnostics or therapeutics.

Method: Peanut flour protein was prepared from roasted and defatted peanut flour using standardized aseptic extraction conditions at pH 7.4. Peanut allergens were quantified in quadruplicate using validated allergen-specific ELISA's (Ara h 1, Ara h 2, Ara h 3, Ara h 6, and Ara h 8) and analyzed by SDS-PAGE, endotoxin assay, and mass spectrometry (LC-MS/MS). Real time stability data were collected from frozen liquid allergens over a period of 24 months.

Results: Peanut flour protein showed excellent reactivity in peanut allergen-specific ELISA assays. Ara h 3 (764 μg/mL) concentrations were the highest, followed by Ara h 6 (257 μg/mL), Ara h 2 (234 μg/mL) and Ara h 1 (190 μg/mL). This pattern was similar to the results obtained by LC-MS/MS. Ara h 3 was the most abundant allergen (61%), followed by Ara h 2 (15%), Ara h 6 (15%) Ara h 1 (7%) and Ara h 7 (1.5%). Abundance of other peanut allergens and non-allergenic peanut proteins was very low (<0.5%). Endotoxin levels were < 0.03 EU/μg. Real time stability tests of frozen liquid allergens (up to 24 months) showed consistent potency in allergen-specific ELISA and no signs of degradation on SDS-PAGE.

Conclusion: Ara h 1, Ara h 2, Ara h 3, and Ara h 6 are the predominant allergens in roasted peanut flour extracted at neutral pH. Optimized, ISO-9001 compliant, bioprocessing pathways have been established to yield standardized peanut flour allergen with defined allergen profiles which can serve as a reference standard.

The low-endotoxin peanut flour protein has applications as a standard for monitoring the composition of peanut diagnostics and therapeutics.

TP0850 | Peamaclein (Pru P 7): Recombinant expression, physicochemical characterization and its application for component resolved diagnosis

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Background: Up to date 6 individual allergens are identified from peach, including class 1 and class 2 allergens. While there is a considerable number of data of class 1 allergens available, less is known about class 2 allergens from peach, including peamaclein. Especially information about allergens responsible for the cypress-peach syndrome is limited. Previously, immunoglobulin E (IgE) cross-reactivity between peach and cypress pollen was shown suggesting that members of the gibberellin regulated protein (GRP) family could be the causative allergens. Therefore, this study aims to produce recombinant Pru p 7 in *P. pastoris*, assess the physicochemical and immunological characteristics of this allergen and to investigate its role as a cross-reactive marker allergen.

Method: Pru p 7 (UniProt: P86888) was expressed in yeast using the N-terminally placed alpha-factor secretion signal followed by a Kex2 cleavage site. This way the expressed protein is secreted with a conserved N-terminus. Purification was performed by cation exchange chromatography. Physicochemical properties of the expressed protein were analysed by N-terminal EDMAN degradation and MALDI-TOF mass spectrometry. Furthermore, the protein was analysed by CD spectroscopy and dynamic light scattering to check secondary structural features.

Results: After successful cloning of rPru p 7 in *P. pastoris* and optimizing expression level (final yield of 2.25 mg/l pure protein) a purification protocol was established and performed. Purified recombinant peamaclein migrates in SDS PAGE as a single band at around 10 kDa. N-terminal EDMAN degradation confirmed its correct amino acid sequence and MALDI-TOF mass spectrometry provided a mass of 6.903 Dalton corresponding to the theoretical mass of 6.910 Dalton. CD spectroscopy provided evidence of a folded protein and dynamic light scattering confirmed that peamaclein is present as a monomer in solution. ELISA and immunoblotting results with a selected pool of peach allergic sera confirmed IgE specific binding.

Conclusion: Recombinant Pru p 7 was produced in a eukaryotic expression system. The application of rPru p 7 will help to assess the prevalence of IgE binding in a cohort of peach allergic patients with and without concomitant inhalant allergies.

TP0851 | Investigation of purity of ovomucoid-specific IgE test kit with mouse-human chimeric IgE antibody

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Background: Component-resolved diagnostics(CRD)is increasing in routine examinations. CRD is clinically applied taking advantage of the characteristics of each component. Therefore, the antigenicity and purity of the components used for CRD are important. Ovomucoid (OVM) is the most routinely used CRD in Japan. Purification of OVM is difficult, and it is reported that lysozyme (LYZ) was contaminated in commercially available purified OVM. The purity of OVM used in a commercially available specific IgE test kit was examined using anti-OVM and anti-LYZ mouse-human IgE chimeric antibodies.

Method: We prepared dilution series of chimeric antibodies against OVM (Gal d 1) and LYS (Gal d 4) prepared by the method of Schuuman et al. Then, using this as a specimen, anti-OVM specific IgE was measured with the ImmunoCAP.

Results: Measurement results of anti-Gal d 1 chimeric antibody showed dilution linearity. And within the measurement range, specific IgE could be measured quantitatively. The results of an Anti-Gal d 4 chimeric antibody were less than detection limit of the test (<0.1 UA/mL) in all dilutions.

Conclusion: Measurement of anti-OVM specific IgE of ImmunoCAP showed sufficient specificity. LYS contamination was not observed in OVM. We also conduct similar studies in other specific IgE test methods and report on the effect of the purity of the OVM of the test kit on clinical diagnosis using actual clinical specimens.

TP0852 | Component-resolved diagnostics can contribute reducing the burden of food allergy among swedish schoolchildren: A population-based simulation study

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Background: Elimination diets due to food allergy remain vastly unmonitored among Finnish children [Palmu 2018, Savolainen 2019]: in fact, special diets are often followed even after tolerance to foods is achieved, generating thus avoidable costs. With a structured diagnostic algorithm including component-resolved diagnostics (multiplex immunoassay) and food-challenges it was possible to reduce special diets by 65% in Finland [Savolainen 2019]. This study aims to quantify the hypothetical cost savings in Sweden by simulating

the nation-wide usage of the same diagnostic intervention among all schoolchildren requesting a special diet at school.

Method: In Sweden, children receive free meals at school. A doctor certificate is required every school year in order to have access to special meals; the yearly additional costs ascribable to special meals are estimated on average as 3 440 SEK per child. In 2017, there were 1 397 533 schoolchildren in Sweden; the model assumes that 12.2% of them had food allergies [Sterner 2018].

In the simulation performed, the effectiveness of our intervention was modelled either as A) 65% [Savolainen 2019] or B) 87.5% [Nilsson 2018]; in both cases 4% of food-challenges were simulated.

Results: 170 499 schoolchildren requested special meals in 2017 in Sweden, costing the State additional 582 million SEK per year.

A) Using the multiplex immunoassay in 42% of children on a diet and assuming 65% effectiveness (as in [Savolainen 2019]), the simulated diagnostic algorithm costed 247 million SEK, thus saving 132 million SEK per year.

B) Using the multiplex immunoassay in all children requesting special school meals and assuming a 87.5% effectiveness (as in [Nilsson 2018]), special diets for 509 million SEK could be avoided, while the proposed intervention costed 484 million SEK.

Conclusion: Our structured intervention which includes component-resolved diagnostics and food-challenges could hypothetically lead to substantial cost savings ranging between 25 and 132 million SEK per year in Sweden.

TP0853 | Estimation of the clinical significance of IgG analyses in atopic and non-atopic patients with food dependent symptoms

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Background: It is stated, that only 50% of allergic reactions to food is mediated by IgE immunoglobulins. Diagnosis of food hypersensitivity in patient with negative skin prick tests and IgE concentration against food allergens, often poses problems due to the different pathomechanism of the immune response. The more and more popular analyses of IgG4 concentration in serum, became the basis of elimination diets. The lack of unambiguous rules for the interpretation of IgG4 results for foods can lead to nutritional deficiencies and loss of tolerance of foods eliminated from the diet. The aim of the study was to assess the clinical relevance of IgG4 concentration for food allergens by means of an elimination diet and re-entering food in patients with hypersensitivity symptoms to these products.

Method: The group of 40 patients (22-56 years, mean 39), who reported symptoms of food hypersensitivity was included into the study, with the exception of IgE-mediated food allergy (negative skin prick tests and/or IgE for food allergens). Patients with atopy (positive skin tests with inhalant allergens) constituted the study group, while in the control group atopy was not confirmed. Patients completed questionnaires and the IgG4 concentrations for food allergens (egg, nuts, casein, fish, peach, gluten) were measured. A 4 week elimination diet was used, including the products of the higher IgG4 level, followed by introduction the eliminated products, one by one every two weeks.

Results: The analyses of the questionnaires showed that the majority of patients (68%) reported skin and digestive symptoms, after consumption of milk, nuts, eggs, fruits and wheat bread. In almost all patients, the higher level of IgG4 against eggs and casein was found (98% and 80% of patients, respectively), with clinical symptoms manifested by about 30% of patients in both groups after eating these products. Up to date, 45% of patients from both groups have finished the whole study procedure, including elimination and the following introduction of the products. In most of them (about 78%), the products of a higher IgG4 level, were well tolerated. On the other hand, some symptomatic patients after food, have presented the low IgG4 level.

Conclusion: Only in about 22% of patients the higher IgG4 level against foods is clinically relevant and allows to eliminate given food products.

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TP0854 | Citrus seed allergy and cross-reactivity

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Case report: Background: Citrus fruits belong to the Rutaceae family of the Sapindale order. They are commonly consumed in foods and drinks. A few core ancestral species have undergone interbreeding and hybridisation to create a wide diversity of hybrid species that are regularly consumed worldwide. Hypersensitivity reactions to citrus seeds are uncommon. We report a case of IgE-mediated hypersensitivity to lemon seed with a demonstrable pattern of cross-reactivity. Method: A 26 year old female presented with nasal congestion, wheeze, throat tightness, generalised urticaria and nausea and vomiting immediately following salad consumption. Her symptoms resolved within 1 hour with oral antihistamine and salbutamol inhalation. She had two further episodes on consumption of salad. A common ingredient in these salads was fresh lemon juice. She however tolerates lemon juice and orange juice in drinks without symptoms. Medical history includes pistachio and cashew allergy. Skin prick tests (SPT) were performed to commercial extracts. Prick to prick tests (PPT) were performed to various citrus fruit species and foods belonging to other families of the Sapindale order.

Results: SPT was negative to peach solution, a surrogate for lipid transfer protein. PPTs were positive to seeds of lemon, limequat and orange: three hybrids derived from citron and/or mandarin orange ancestral species. PPTs were negative to the peel and flesh of lemon, orange and

limequat. PPTs were negative to the seed, peel and flesh of grapefruit, clementine, bergamot pomelo and kumquat. Pomelo and kumquat are ancestral non-hybrid species. PPTs were positive to mango seed, cashew nut and pistachio nut (all three belonging to the Anacardiaceae family). PPTs were negative to mango peel and flesh. PPTs were negative to lychee peel flesh and seed (belonging to the Sapindaceae family). Conclusion: We report a case of lemon seed allergy with a pattern of greater seed cross-reactivity between citrus hybrids with shared ancestral species origins. In the presented case the shared ancestral species are citron and mandarin orange. Negative PPT to bergamot, which share similar species ancestry, may be due to the underdeveloped seeds present in the bergamot fruit used. We also demonstrate cross-reactivity between seeds of two families of the Sapindale order: the Anacardiaceae and Rutaceae family. This suggests cross-reactivity with members of the Anacardiaceae family should be explored in citrus seed allergic patients.

TP0855 | Recombinant Ses i 1 - a useful diagnostic marker in sesame allergy

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Background: Sesame allergy is an emerging allergy of increasing importance, often appearing early in life and persisting into adulthood. Symptoms range from mild to severe and life-threatening anaphylaxis. Currently available tests based on natural sesame extract comprise a variety of IgE binding determinants, including cross-reactive moieties of low clinical relevance. This may lead to overdiagnosis and unnecessary food restrictions. Ses i 1 is a major sesame allergen belonging to the 2S albumin family, a class of food allergens of well recognized clinical importance. 2S albumins from different nuts and other seeds are divergent in primary structure and generally show little cross-reactivity between species. Ses i 1 only shares 27-50% sequence identity with 2S albumins in peanut, walnut, hazelnut, cashew nut, brazil nut and buckwheat. Hence, it has the potential to serve as a highly specific reagent in the diagnosis of sesame allergy. The aim of this study was to generate and immunologically evaluate recombinant Ses i 1.

Method: Recombinant Ses i 1 was expressed as a hexahistidine tagged protein in *Pichia pastoris* and purified by immobilized metal ion affinity and ion exchange chromatography. The identity was confirmed by mass spectrometry (MS/MS) using an Orbitrap Fusion instrument. IgE antibody responses to natural sesame extract and rSes i 1 were measured by ImmunoCAP in sera of 27 sesame allergic subjects.

Results: Recombinant Ses i 1 was expressed at an intermediate level and purified to final yield of approximately 65 mg per liter of *P. pastoris* culture. The Ses i 1 preparation formed one distinct band of expected size in SDS-PAGE and a single, symmetrical peak in analytical gel filtration consistent with a monomeric state. Its identity was confirmed by MS/MS and no remaining host cell proteins were detected. All sesame allergic subjects showed IgE binding to rSes i 1. The measured IgE levels correlated strongly ($r = 0.90$) with those to sesame extract and were of comparable magnitude. Since IgE antibodies reactive to pollen-related, cross-reactive components will not recognize rSes i 1 but often bind to components in sesame extract, rSes i 1 can be expected to provide for improved diagnostic specificity.

Conclusion: Recombinant Ses i 1 could be produced in *P. pastoris* in a fully immunoreactive form. IgE to Ses i 1 showed 100% clinical sensitivity in the study population and is an important addition to the panel of allergens useful in the diagnosis of allergy to sesame seeds.

TP0856 | Ana O 3 is a reliable marker for cashew nut allergy in adults

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Background: The prevalence of cashew allergy seems to be increasing due to a higher frequency of cashew nut consumption. Detection of sIgE to Ana o 3 and to a lower extent to Ana o 1 and 2 increases the accuracy of diagnosing cashew nut allergy in children compared to the extract. However, it is not known whether cashew nut components have an additional value in diagnosing cashew nut allergy in adults.

Method: Sensitisation to cashew nut extract and components was evaluated by line blot (EUROLINE, EUROIMMUN, Luebeck, Germany) in retrospectively selected sera of cashew nut allergic (n = 38) and tolerant patients (n = 30) confirmed by open food challenge or convincing history.

Results: Specific IgE to cashew nut extract and Ana o 3 were significantly elevated in cashew nut allergic patients compared with the tolerant group (cashew nut extract: $P < 0.0001$; Ana o 3: $P = 0.0007$). Overall, the mean of EUROLINE-intensity detected for cashew nut extract (30; EAST class 3) was higher than for Ana o 3 (13; EAST class 2). By means of Ana o 3, a 100% positive predictive value was achieved for 53% of the patients at an EUROLINE-intensity of 3 (EAST class 1), corresponding to the test related cut off. Specific IgE to Ana o 1 and 2 were detected in a low number of allergic (Ana o 1: 11%; Ana o 2: 18%) and in some tolerant patients (Ana o 1: 3%; Ana o 2: 7%). However, 24% of cashew nut allergic patients, mostly suffering from OAS or dyspnoea, did not show sensitisation to neither cashew nut extract nor single components. No significant difference of sIgE levels for neither cashew nut extract nor Ana o 3 was observed between patients with mild, moderate or severe symptoms.

Conclusion: Ana o 3 is a reliable marker for diagnosing cashew nut allergy in adults and could replace food challenges for this purpose in Ana o 3 sensitized patients.

SUNDAY, 2 JUNE 2019
TPS 14
URTICARIA AND ANGIOEDEMA I

TP0857 | IgE anti-TPO as a biomarker of different clinical phenotypes in chronic spontaneous urticaria

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Background: IgE antibodies against thyroid-peroxidase (anti-TPO IgE) have been demonstrated in a group of CSU patients in higher frequency that healthy subjects. However, the clinical impact of these IgE autoantibodies it′s still a matter of study. The aim of this study, was to evaluated different clinical characteristics among CSU patients, according to the presence or not of anti-TPO IgE in serum, during periods of clinical control (Urticaria activity score, 0 points) or urticaria exacerbation (≥3 points).

Method: One-hundred CSU patients from the URTICA cohort (ClinicalTtrials.gov number: NCT01940393) participated in the study participated in the study. The levels of anti-TPO IgE were measured during clinical control period and exacerbation period. Patients with self-report of skin exacerbation by foods, nonsteroidal anti-inflammatory drug (NSAIDs) or physical triggers were subjected to a controlled challenge test.

Results: According anti-TPO IgE, we identify four groups; patients with anti-TPO IgE during clinical control period (n = 12), patients with anti-TPO IgE during clinical control and increase levels during exacerbation period (n = 18), patients with anti-TPO IgE only during exacerbation period (n = 13) and patients without anti-TPO IgE during control or exacerbation period (n = 57). Patients from the three groups with anti-TPO IgE in some period, had a higher frequency of atopy, asthma, and positive challenge test with NSAIDs. Patients without anti-TPO IgE (four group), had a higher frequency of positive challenge test for physical activities. Sixty-four (64%) patients reported a reaction with one o more foods, but none of them had (+) challenge test.

Conclusion: We observed different clinical characteristics according to the presence or absence of anti-TPO IgE; therefore, these auto-antibodies could serve as clinical biomarkers. Furthermore, the elevation of anti-TPO IgE during exacerbation periods, supports a possible association between this autoantibody and the pathogenesis of urticaria.

TP0858 | Systemic and local evidence for complement involvement in chronic spontaneous urticaria

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Background: There are still many uncertainties about the pathogenesis of chronic spontaneous urticaria (CSU) and the mechanism of action of omalizumab in CSU remains unclear. We hypothesized a role for the complement system given the fast clinical response to omalizumab. Therefore, we assessed the role of complement factors in adults prior to and during treatment with omalizumab.

Method: 30 CSU patients were treated with 6 administrations of 300 mg omalizumab every four weeks followed by a follow-up period of 12 weeks. Patient-reported outcomes were assessed at various time points, using the UAS7 and the UCT. Complement activity, e.g. C1q, C3, C3bc/C3, C4, C4bc/C4, C5a and MAC in peripheral blood were analyzed and complement activation in the skin was determined by the analysis of C4d deposition. Results were furthermore related to the clinical response to omalizumab.

Results: Lesional skin biopsies revealed complement deposition (C4d) at baseline in blood vessels in the papillary dermis of 53% (16/30) of the patients, which suggests involvement of immune complexes in the pathogenesis of urticaria. C5a levels at baseline were elevated compared to healthy controls (P = 0.010), indicating increased complement activation in urticaria.

Conclusion: C4d deposition in lesional skin indicates the involvement of immune complexes in the pathogenesis of CSU and elevated C5a levels indicate increased complement activation in CSU.

TP0860 | Efficacy and safety of omalizumab in patients with chronic inducible urticaria

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Background: Chronic inducible urticarias (CIndUs) are frequently antihistamine resistant and the avoidance of the eliciting triggers is usually unfeasible. Since 2006 omalizumab has been used off-label for the treatment of different types of refractory CIndUs. The aim of the study is the assessment of the efficacy and safety of omalizumab in the treatment of 12 patients with CIndUs.

Method: We performed an analysis of medical records of 12 patients with CIndUs (8 male, age range 18-70 years) treated with omalizumab in our department from November 2009 until December 2018. Patients were diagnosed with cold urticaria (n = 4), cholinergic urticaria (n = 4), cold urticaria and cholinergic urticaria (n = 3) and symptomatic dermographism (n = 1). They received 150-300 mg omalizumab every 4 weeks, due to unresponsiveness to antihistamine treatment. We assessed rates and time of response, time of relapse after discontinuation of therapy and safety of the drug.

Results: Complete response was achieved in 5 (41.6%) patients and significant improvement in 6 (50%). Only 1 patient had no significant improvement, but he dropped out after the first injection. The interval between doses was extended to 6-8 weeks in 8 (66.6%) patients. The median time of response was 1 month (range 1-4). As for the ice cube test performed in patients with cold urticaria, an increase in time needed to elicit response during the treatment with omalizumab was noticed.

The serum total IgE level was 393 (3-1081) IU/mL (median with range). In complete responders the median total IgE was 394 (316-837) IU/mL, while in partial responders was 50 (3-1081) IU/mL.

Six patients discontinued the treatment (1 drop out, 5 in accordance with our treatment plan). After the discontinuation of omalizumab 1 patient with cold urticaria and 1 patient with cholinergic urticaria have no relapse 6 and 16 months later respectively. In contrast 2 patients with cold and cholinergic urticaria had a relapse of cholinergic urticaria 6 and 16 months after the last administration of omalizumab, while both have no relapse of cold urticaria yet. One patient was lost to follow up. There were no reports of adverse reactions.

Conclusion: According to our study omalizumab is an effective and safe treatment for refractory CIndUs. 91.6% of patients achieved complete or significant remission and the drug was well tolerated. Randomized placebo-controlled trials are needed to confirm the efficacy and safety of omalizumab in the treatment of CIndUs.

TP0861 | Chronic urticaria—What about montelukast?

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Case report: A significant proportion of patients with chronic urticaria respond inadequately to first line treatment with antihistamines. Leukotriene receptor antagonists (LTRA) have been used for chronic urticaria but, according to the latest guidelines, the evidence for prescribing this drug class is weak.

We present a 41 year-old female with daily urticarial lesions for 3 years, sometimes associated with facial edema. In 2014 she had a full laboratorial work-up that was negative for auto-immune, thyroid and complement disorders, as well as for infectious diseases. She had been prescribed daily treatment with different anti-histamines (anti-H1 double dose plus anti-H2) and corticosteroids, with no possibility of reducing the dose due to recurrence of symptoms. In 2016 she was also prescribed cyclosporine (100 + 100 mg/day) with no response. In 2017 she was referred to our clinic and by then she was under prednisolone 20 mg/day and bilastine 40 mg/day, with symptoms recurring every time she tried to reduce the dose of either drug. Before considering step-up to omalizumab, we decided to try levocetirizine 15 mg/day plus montelukast 10 mg/day together with prednisolone tapering. After two months treatment, the patient's urticaria was controlled, with no further need for prednisolone. Later, by mistake, the patient stopped taking montelukast and 4-6 weeks later she needed to restart therapy with prednisolone, due to urticaria recurrence. We advised her to restart montelukast and she was once more able to withdraw corticosteroid therapy. Presently, she remains symptom free, under montelukast 10 mg/day and levocetirizine 10 mg/day.

This case is in accordance with other reports in literature, showing that montelukast can be considered an appropriate second-line agent in selected cases of chronic spontaneous urticaria, especially in patients with angioedema-associated disease. Written consent to share clinical information was given by the patient.

TP0862 | Effectiveness in treatment of solar urticaria with omalizumab: A case report

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Case report: Solar Urticaria (SU) is an uncommon chronic inducible urticaria that represents 0.08-0.4% of the total urticaria cases. The main trigger is solar radiation causing immediate intense pruritus or burning erythema flare on the exposed skin. In recent years, a few cases have been reported in which the effectiveness of the omalizumab treatment in the Solar Urticaria has been tested. We present the case of a patient for which we have collected epidemiological and clinical data, IgE levels and recorded the response to treatment with omalizumab: A 57-year-old woman with pruritic erythema in skin areas which have been exposed to the sun, at all year seasons, for more than 5 years. The lesions appeared at 5-10 minutes of sun exposure and disappeared spontaneously at 30-60 minutes. She was previously treated with bilastine at maximum doses with poor response.

Method: We studied the patient from different allergological points of view and perform the following tests:

1) urticaria analytical protocol
2) standard allergen battery (pneumoallergens, food)
3) phototest (visible light)

4) Urticaria Activity Score (UAS7)

Results: The results of skin prick-test and blood test were negative, the phototest (visible light) was positive after 5 minutes of exposure and the UAS7 before treatment was 17.

The patient was diagnosed with poorly controlled Solar Urticaria and we decided to start with omalizumab 300 mg/month for 6 months. After completing the 6-month treatment cycle, the patient obtained a complete response with negativization of phototest (visible light) and UAS7 was 5.

Conclusion: Omalizumab can be an effective and safe treatment line in the SU refractory to treatment with anti-histamines

The response dose in the patient is the same dose as approved in the data sheet for Chronic Spontaneous Urticaria (300 mg/month).

TP0863 | Concentration of vitamin D receptors (VDR) of mononuclear blood cells and level of total IgE in patients with chronic spontaneous urticaria

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Background: Experiment revealed interaction between expression of specific receptors to vitamin D (VDR) by lymphocytes and IgE level in the blood serum (James, 2017). On the other hand, potential risk factor for development of chronic spontaneous urticaria (CSU) could be polymorphism of VDR genes (Nasiri-Kalmarzi, 2018).

Aim: to study VDR concentration of mononuclear blood cells in patients with CSU and determine if there is a correlation between VDR content and total IgE level in the patients' blood serum.

Method: the study involved 25 patients with CSU — 8 males (32.0%) and 17 females (68.0%) of the average age of 45.7 ± 3.31 years. Control group included 28 healthy donors — 6 males (21.5%) and 22 females (78.5%) of the average age of 40.1 ± 2.44 years. VDR concentration of mononuclear cells in the peripheral blood was determined by ELISA. Mononuclear cells were isolated with sedimentation in a single-stage density gradient ficoll-urografin by Boyum (1968). Blood was collected from the examined individuals for 3 months (from February to April) to reduce seasonal effects on the VDR content. Concentration of total IgE in the blood serum was determined with the solid-phase chemiluminescent enzyme immunoassay method. The range of normal IgE values is 0-100 IU/mL. Depending on the content of IgE patients were divided into 2 groups. Group 1 included 13 patients with CSU and concentration of IgE in the normal range (average IgE level — 38.8 ± 10.18 IU/mL), group 2 included 12 patients with an IgE level higher than the upper limit of the norm (average IgE level— 242.1 ± 29.07 IU/mL). Descriptive statistics was analyzed using the mean and the mean error (M ± m).Calculation of the significance level (p) was performed with the Mann-Whitney test, the correlation analysis was wade by Spearman method.

Results: VDR concentration of mononuclear blood cells in patients with CSU did not differ from the data in the control group (1.1 ± 0.25 ng/mL and 0.69 ± 0.08 ng/mL, $P > 0.05$). VDR concentration in group 1 was 0.75 ± 0.14 ng/mL and in group 2 it was 1.5 ± 0.49 ng/mL ($P > 0.05$). In patients with CSU of both groups linear correlations between VDR concentration of mononuclear blood cells and the level of total IgE in the blood serum were not found.

Conclusion: VDR concentration of mononuclear blood cells in patients with CSU does not differ from control data and does not correlate with the level of total IgE in the blood serum.

TP0864 | Dupilumab as a novel therapy for difficult to treat chronic spontaneous urticaria

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Case report: Background: Chronic spontaneous urticaria (CSU) is a condition marked by episodes of elevated, pruritic, red wheals persisting for more than 6 weeks without a specific known cause. Many treatment options exist for CSU including omalizumab, a monoclonal anti-IgE antibody approved for atopic dermatitis; however, it may not be effective in all cases. Here we present six cases in which dupilumab controlled CSU in those who have previously failed on omalizumab.

Method: Six patients presented with chronic urticaria episodes with durations that ranged from 2-12 years with baseline urticaria activity scores (UAS) ranging from 31-38. Despite treatment with varying concomitant medications as well as increasing doses of omalizumab up to 600 mg monthly, their UAS scores remained unchanged. Consequently, a decision to commence dupilumab treatment was made.

Results: Within 3 months of commencing dupilumab treatment, the durations and severities of each patients' chronic urticaria episodes resolved completely on a 600 mg subcutaneous loading dose followed by 300 mg of subcutaneous dupilumab every two weeks. One of the patients has a unique history of failing both omalizumab 600 mg subcutaneous monthly and canakinumab monthly but responded quickly to dupilumab.

Conclusion: Here we present the first reported cases to our knowledge in which dupilumab controlled CSU in multiple patients who have previously failed to improve on omalizumab despite dosing up to 600 mg monthly with adjunctive medications. This report strongly suggests that dupilumab's potential role in CSU warrants further study through a randomized control trial.

Funding: Evidence Based Medical Educator Inc.

Statement of consent: Consent to publish was obtained from the patients involved in this study.

TP0865 | The management of acute urticaria, a systematic review

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Background: To date, only few clinical trials addressed the management of acute urticaria. Especially, the added value of systemic corticosteroids to antihistamines is unclear in treatment of severe acute urticaria. Objective of this study was to review the existing evidence-based approaches for management of acute urticaria.

Method: A systematic electronic search was done in PubMed, Embase and Web of Science to retrieve all studies on management, treatment and diagnosis of patients with acute urticaria. Two reviewers included eligible randomized controlled trials (RCT), treatment protocols, practice guidelines on acute urticaria and data was. A descriptive synthesis was conducted in line with the PRISMA statement. Quality assessment was independently performed by both reviewers ("Cochrane Risk of Bias tool" for RCTs; AGREE II for guidelines).

Results: Eight RCTs (n = 520 participants) and 9 guidelines were included. Three studies assessed the effectiveness of corticosteroids added to antihistamines and 5 studies compared the efficacy of H_1 and/or H_2-antihistamines for the treatment of acute urticaria. Prednisone (20 mg for three days or 50 mg for four days PO) combined with loratadine (10 mg, PO) or diphenhydramine (50 mg, IM) respectively, was shown to improve pruritus and cessation of wheals in 2 out of 3 RCTs. The combination of diphenhydramine (50 mg, IV) and ranitidine (50 mg, IV) or cimetidine (300 mg, IV) was most efficient for relief of urticaria in 2 out of 5 studies. Sedation and drowsiness were the most frequent adverse effects. All guidelines recommend once daily H_1-antihistamine as standard first-line therapy. Five guidelines recommend to increase the dose up to four-fold in non-responders, and 4 guidelines recommend the addition of an H_2-blocker if treatment with H_1-blockers is insufficient. A short course of oral corticosteroids was recommended in all guidelines for unresponsive patients with severe acute urticaria.

Conclusion: The few available guidelines included in this review mainly focus on chronic- than on acute urticaria. In addition, only few, small RCTs provide evidence for the management of acute urticaria. Thus, the state-of-the-art management of this frequent condition remains unclear. Well-designed, high-quality interventional trials are needed to establish evidence-based treatment guidelines for acute urticaria.

TP0866 | Questionnaire to evaluate the first-generation antihistamine side effects in patients with chronic spontaneous urticaria

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Background: Chronic spontaneous urticaria (CSU) is characterized by the sudden, continuous or intermittent appearance of pruritic wheals, angioedema, or both for six weeks or more, with no known specific trigger. It's a disease that can interfere considerably with patients' quality of life (QoL). The first-line treatment for the patient with CSU is the second-generation H1-antihistamine (AH1). However, in some countries, first-generation AH1 is still prescribed for economic reasons. The objective of the study was to create a questionnaire to assess the side effects related to the first-generation AH1.

Method: Development and application of a questionnaire to assess the potential side effects related to first-generation AH1 (QAH), hydroxyzine. Adult patients with CSU were included in follow-up at a tertiary hospital. The questionnaire included 10 questions regarding 1) sleep disorders, 2) tiredness upon awakening, 3) daytime drowsiness, 4) dizziness, 5) forgetfulness, 6) work productivity, 7) hunger, 8) dry mouth, 9) dry eye, and 10) memory disorders. The final results (in %) were compared to the quality of life questionnaire, CU-Q2oL (%). Subsequently, the patients were classified according to the frequency of side effects related to AH1 (≤40% and > 40%).

Results: There were included 67 patients with CSU, 95.5% were female, the mean age was 50.2 years and disease time was 12.7 years. Thirty-five patients (52.2%) were taking other drugs than AH1 (first- and second-generation) to control CSU. The mean dose of hydroxyzine used was 28.4 mg per day. The mean frequency of side effects related to hydroxyzine was 33.5%. The main side effects related to AH1 were tiredness upon awakening, daytime drowsiness, forgetfulness and dry mouth. There was a correlation between the results of the QAH and CU-Q2oL questionnaires ($r^2 = 0.36$, $P < 0.001$). When comparing the two groups (≤40% versus > 40%), we did not find differences in demographic characteristics and in dose of hydroxyzine; however, the group with more side effects required more often other therapies added to hydroxyzine ($P = 0.07$) and a worse QoL ($P < 0.001$).

Conclusion: Despite the first-generation AH1 were withdrawn from CSU guidelines, they are still important to manage this disease in some countries and knowing which patients are able to tolerate using first generation AH1, can provide a good cost effective treatment with positive impact in the QoL.

TP0867 | Treatment of cold urticaria with omalizumab at the Hospital Universitario de Guadalajara (Spain)

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Background: Cold urticaria is a rare form of physical urticaria usually characterized by the appearance of wheals after exposure to cold, although in some cases systemic symptoms like anaphylaxis may also occur. Second-generation anti-H1 antihistamines are the first line of treatment in cold urticaria. However, there are cases resistant to this treatment. Several case reports suggest that patients with cold urticaria resistant to antihistamine treatment can benefit from treatment with omalizumab (a recombinant humanized anti IgE antibody). In this study, we evaluated the efficacy of omalizumab treatment in patients with cold urticaria at the Hospital Universitario de Guadalajara.

Method: We included patients with acquired cold urticaria resistant to anti H1 antihistamine treated with omalizumab in follow-up by the Department of Allergy of the Hospital Universitario de Guadalajara from 2009 to 2018.

Eight patients were studied (6 women, 2 men).

Median age 26.75 years (12-44 y): All patients had urticaria after exposure to cold. Five patients (62.5%) had severe cold-induced urticaria (urticaria+systemic symptoms).

Six of them (75%) reported a history of atopy (allergic asthma, allergic rhinitis or food allergy).

Initial dose of omalizumab: 150 mg/month in 4 patients, 300 mg /month in 2 patients, 600 mg /month in 1 patient and 300 mg /15 days in 1 patient.

Results: Total or partial control of symptoms was observed in 83.33% of the cases.

Complete response: 75%

Partial response: 12.5% (dose 300 mg /month)

No response: 12.5% (dose 150 mg/month)

In patients with partial response and no response the dose of omalizumab was increased, without finding any clinical improvement.

Conclusion: There are few studies on the treatment of cold urticaria with omalizumab and these studies include few patients. Currently published data indicate total symptom control from 44% in the largest cohort to 100% in other studies. In our experience, omalizumab is an effective treatment in most patients with cold-induced urticaria who do not respond to antihistamine therapy.

TP0868 | Efficacy of omalizumab in a patient with chronic spontaneous urticaria and several subtypes of inducible urticaria

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Patient	Gender	Age	Symptoms with cold	Ice cube test before treatment	Serum cryoglobulin/ crioaglutininas	Personal history of atopy	Total IgE (UI/mL)	Omalizumab: start year	Omalizumab: start dose (mg/month)	Response
1	Female	13	Urticaria and anaphylaxis	Positive	Negative	Allergic asthma Food allergy	747	2009	300	PARTIAL
2	Female	26	Urticaria	Positive	Negative	Allergic asthma Food allergy	645	2009	300/15 days	YES
3	Female	38	Urticaria	Positive	Negative	Allergic rhinitisAllergic asthma	416	2012	600	YES
4	Female	20	Urticaria	Positive	Negative	Oral allergy syndrome	198	2013	150	YES
5	Male	12	Urticaria and anaphylaxis	Positive	Negative	Negative	50	2014	150	NO
6	Male	44	Anaphylactic shock	Positive	Negative	Negative	179	2014	300	YES
7	Female	40	Urticaria and anaphylaxis	Positive	Negative	Allergic rhinitis	322	2015	150	YES
8	Female	21	Urticaria and anaphylaxis	Positive	Negative	Allergic rhinitis	1201	2016	150	YES

Case Report

Background: Currently, omalizumab, a humanized monoclonal anti-IgE antibody, is a third-line treatment of chronic spontaneous urticaria (CSU) in patients with poor response to second generation antihistamines. However, the evidence supporting its use in chronic inducible urticaria (CIndU) alone or in combination with CSU is limited. Here, we describe efficacy of omalizumab in a patient with CSU and several subtypes of CIndU: symptomatic dermographism, delayed pressure urticaria and cholinergic urticaria.

Case: A 28-year-old female was admitted to our Department with CSU and CIndU which occurred two years ago. Itchy wheals with or without angioedema appeared spontaneously or after rubbing or scratching of the skin, intake of alcohol, emotional stress, hot shower, and sustained pressure on the skin. The diagnosis of CSU and CIndU was made in accordance with the clinical guidelines. Provocation tests included the Fric Test device, a bag with 5 kg suspended on the shoulder and hot bath. The patient had active (UAS7 = 42) and uncontrolled disease (UCT = 11) and the quality of life was significantly decreased (DLQI = 15, CU-Q2oL = 51%). ESR, total IgE, ECP and CRP were within reference intervals. Symptoms did not respond to high doses of second generation antihistamines. Two weeks after injection of omalizumab 300 mg the patient experienced total remission of her CSU and CIndU. A month after the injection, all provocation tests were completely negative and the patient showed significantly decreased disease activity and quality of life was improved (UAS7 = 2, UCT = 15, DLQI = 2, CU-Q2oL = 82%). No adverse effects were seen.

Conclusion: Concomitant CindU is seen in up to 40% of CSU patients. Our case indicates that patients with both CSU and several subtypes of CindU can benefit from omalizumab treatment. Further prospective studies involving a large number of patients are required.

TP0869 | Evaluation of clinical characteristics and autoreactivity in CSU patients by ASST and BAT

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Background: Autoreactivity diagnosis in chronic spontaneous urticaria(CSU) can predict a more prolonged disease course, higher disease activity and a different response pattern to therapy. Autoreactivity can be studied by the autologous serum skin test(ASST) and the basophil activation test(BAT). Objective: Clinical characterization of patients (pts), and their comparison, according to their positivity on the ASST and BAT.

Method: Prospective study of 91 CSU pts according to demographic, clinical and laboratorial data. Statistical analysis(SPSS V.23): descriptive statistics, chi-square, Pearson correlation coefficient, kappa correlation coefficient, odds ratio, student test and ROC curve.

Results: 91 pts were included, mean age 46 ± 16 years, 17(19%) male. Clinically, 44(48%) had angioedema, 55(60%) nocturnal symptoms, 24(26%) anti-TPO/Tg antibodies, 9(10%) other autoantibodies, 11(12%) hypothyroidism, 40(44%) lesions which lasted > 5 hours. Average UAS7 was 18 ± 11, UCT 9 ± 4, DLQI 8 ± 6, total IgE 248 ± 715 kU/L.

Autoreactivity was found in 34(35.3%) pts by the ASST and 39(43%) pts by the BAT. The ASST and BAT showed good correlation with each other (OR 11.071, kappa 0.497, $r = 0.512$, $P < 0.01$).

The ASST and BAT showed an association to characteristics of more severe CSU: angioedema($P < 0.05$), nocturnal symptoms($P < 0.05$), symptoms > 5 days/week($P < 0.05$), lesions lasting > 5 hours($P < 0.05$), therapy with montelukast($P < 0.05$), need for omalizumab therapy($P < 0.05$), higher average DLQI(9.4 ± 7.0 in ASST, 8.6 ± 7.0 in BAT, $P < 0.05$), UAS7(22.3 ± 10.4 in ASST, 20.7 ± 10.4 in BAT, $P < 0.05$), lower UCT(7.5 ± 3.9 in ASST, 8.0 ± 4.0 in BAT, $P < 0.05$), and lower IgE in BAT(87.7 ± 90.1 kU/L, $P < 0.05$).

A positive ASST had the highest negative predictive value for positive BAT(68.9%).Combined positive ASST and presence of angioedema had a sensitivity of 48.7% and specificity of 91.7% for positive BAT. Anti-Tg/TPO combined with positive ASST had a specificity of 100% for positive BAT.

ROC curve(area under curve 0.825, $P < 0.01$) shows that the characteristics ASST, angioedema, nocturnal symptoms, symptoms > 5 days/week, Anti-Tg or TPO and UAS7 > 16 have a good discriminant power at identifying a positive BAT result.

Conclusion: Presence of autoreactivity diagnosed either by the ASST or the BAT is an important diagnostic indicator of disease severity and the need for omalizumab therapy. ASST – in association with angioedema, nocturnal symptoms, symptoms > 5 days/week, Anti-Tg/TPO and UAS7 > 16 – can be a surrogate markers of BAT positivity.

TP0870 | Omalizumab versus cyclosporin-A for the treatment of chronic spontaneous urticaria: Are there specific patient characteristics or biomarkers to indicate response to treatment?

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Background: The international guidelines recommend omalizumab (oma) as a first line choice in antihistamine resistant chronic

CSU	Total (n = 95, %)	omalizumab responder n:40, %42.1	cyclosporine responder n:12, %12.6	omalizumab-cyclosporine responder n:23, %24.2	Non-responder n:20, %21.1
Age in years Min-Max (Median) mean ± sd	16-73 (40) 40.94 ± 12.22	27-60 (42.5) 43.18 ± 9.54	16-73 (39) 40.25 ± 17.55	21-66 (33) 37.26 ± 12.17	20-69 (41) 41.10 ± 13.24
Gender n (%)					
Male	32 (%33.7)	16 (%40)	5(%41.7)	9 (%39.1)	2 (%10)
Female	63 (%66.3)	24 (%60)	7(%58.3)	14 (%60.9)	18 (%90)
Accompanying CINDU n (%)	n:84 15 (%17.9)	n:36 7 (%19.4)	n:12 2 (%16.7)	n:16 2 (%13.3)	n:20 4 (%20)
Disease duration (months) Min-Max (Median) mean ± sd	2-402 (30) 59.84 ± 72.94	2-300 (30) 62.42 ± 74.61	3-120 (48) 51.67 ± 40.26	0-264 (24) 52.13 ± 65.06	5-402 (30) 68.45 ± 94.07
Positive ASST n (%)	n:67 41 (%61.2)	n:30 18 (%60)	n:7 5 (%71.4)	n:16 9 (%56.2)	n:14 9 (%64.3)
Positive family history n (%)	10 (%10.5)	2 (%5)	3 (%25)	3 (%13)	2 (%10)
High levels of CRP	n:73 13 (%17.8)	n:31 6 (%19.4)	n:8 3 (%37.5)	n:20 3 (%15)	n:14 1(%7.1)
Angioedema, n (%)	52 (%54.7)	24 (%60)	7 (%58.3)	7 (%30.4)	14 (%70)
Serum total IgE levels^3 100 (IU/mL)	n:79 52 (%65.8)	n:36 24 (%66.7)	n:9 6 (%66.7)	n:17 12 (%70.6)	n:17 10 (%58.8)
Serum total IgE levels (IU/mL)	2.03-6350 (165) 396.46 ± 785.11	3.50-6350 (167) 515.49 ± 1086.06	2.03-1282 (388) 423.43 ± 419.72	6.43-1606 (150) 266.71 ± 375.10	9-1434 (127) 259.89 ± 354.93
High levels of anti-TPO antibody n (%)	n:57 19 (33.3%)	n:22 8 (%36.4)	n:5 2 (%40)	n:18 4 (%22.2)	n:12 5 (%41.7)
Positive h. pylori antigene in the stool examination n (%)	n:73 28 (%38.4)	n:34 13 (%38.2)	n:9 3 (%33.3)	n:18 7 (%38.9)	n:12 5 (%41.7)
Baseline UCT Min-Max (Median) mean ± sd	n:68 0-16 (6.5) 6.97 ± 4.29	n:34 1-16 (6) 6.91 ± 4.50	n:5 2-9 (3) 4.80 ± 3.03	n:14 3-16 (8) 9.20 ± 3.93	n:14 0-11 (5) 5.50 ± 3.74

spontaneous urticaria (CSU). In patients who fail on oma treatment after a trial of 6 months, cyclosporine-A (cyc-A) is recommended as the second step. This step-wise algorithm might be time-consuming and costly. Biomarkers or clinical characteristics which indicates treatment success in CSU patients before starting a specific drug would be very useful in the clinical setting. We aimed to determine if specific patient characteristics or laboratory markers could be used as indicators of oma response or cyc-A response in CSU patients.

Method: We retrospectively analysed patient files of 6 centers which are experienced in treating CU patients. The inclusion criteria for CSU patients was to receive a trial of both oma and cyc-A treatment (not concurrently) long enough (at least 3 months) to decide if there was response to treatment or not. Four groups of patients were defined; patients who respond to oma, patients who respond to cyc-A, patients who respond to both and patients who do not respond to either drug. We analyzed clinical characteristics and laboratory markers of the patients and performed a comparison between groups.

Results: A total of 95 patient files were reachable from 6 centers. Of these 40 (42.1%) were oma responders, 12(12.6%) were cyc-A-responders, 23 (24.2%) were both oma and cyc-A responders and 20(21.1%) were non-responders to both. When oma-responders and cyc-A-responders were compared, no differences were found with respect to age, accompanying inducible urticaria, presence of angioedema, duration of disease, ASST positivity, CRP, ESR, total IgE, anti-tpo, H.pylori, autoimmune thyroiditis and baseline UCT ($P > 0.05$). Non-responders to both drug had a higher frequency of having angioedema compared to responders to both drugs (70%vs30.4%, $P = 0.01$).

Conclusion: We found no specific patient characteristics or clinical markers to define omalizumab or cyclosporine responders in CSU. Markers other than total IgE levels or ASST such as basophil histamine release assay are needed to determine responders of the specific drugs.

TP0871 | How to manage omalizumab in a relapse of chronic spontaneous urticaria?

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Background: Omalizumab (OMZ) indication as an adjunctive treatment of chronic spontaneous urticaria (CSU) which did not respond to antihistamines is well documented and recommended by the EAACI/GA2LEN/EDF/WAO. However, when Omalizumab is discontinued, many patients suffer from new episodes of urticaria at variable intervals of time, which appropriate management remain still unclear. Our aim is to describe, how many patients suffered from a relapse of those treated with OMZ, as well as their most relevant phenotypes characteristics.

Method: A case series was performed with patients who were admitted to our Allergy Department in the last 8 years. Inclusion criteria were: 1) patients treated with OMZ that remained asymptomatic and it was possible to withdraw it. 2) patients who suffered from a recurrence of symptoms a variable period of time, and 3) not responded to high-dose second-generation antihistamines, after relapse. A variable initial dose of 150- 300 mg every four weeks was administered. Decreasing of dose and the final withdrawn of the treatment was done following the protocol previously established in our department. Evaluation of symptoms was estimated with Urticaria Activity Score (UAS) 7 and Urticaria Control Test (UCT).

Results: We report 10 cases from a total number of 60 patients treated with OMZ, 7 of them were women, with a global median of 39.5 years. They remained asymptomatic during a variable time, from 2 months to a maximum of 22 months. Two patients out of three who were asymptomatic longer, before relapse, do not associate angioedema. Meanwhile, patients that were no longer than 2 months released of symptoms, associated angioedema to CSU. Between the last dose of OMZ and its reintroduction, they remained asymptomatic for a variable time: 5 patients for at least 2 months, another patient, 7 months; 1 remained asymptomatic 11 months; and 3 patients for more than one year. Retreatment lasted from 8 months to 4 years, according to recurrence of their symptoms after dose reduction.

Conclusion: We observed, that a drastic reduction of symptoms after the first dose of OMZ, maintained patients asymptomatic a longer time, enabling us to withdrawn treatment before. Probably, patients who suffer CSU and angioedema tend to need a longer prescription of omalizumab. Also, they remained a shorter period of time asymptomatic. Otherwise, controlled studies are required to investigate if there exists some relationship.

TP0872 | Two autoimmune diseases in addition to chronic spontaneous urticaria in an adolescent

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Case report: Background: A 13-year-old boy was referred to our clinic with a 3-month history of chronic spontaneous urticaria (csU). He suffered from recurrent wheals, swelling of the lips, and from diarrhea. A medical examination revealed an increased titer of thyroid- stimulating hormone (TSH), IgG thyroid peroxidase (TPO)-autoantibodies (AAb), and decreased levels of the free thyroxine (fT4). The levels of triiodothyronine (fT3), thyroglobulin-AAb and thyroid stimulating hormone receptor-AAb were in the normal range. Thyroid ultrasound showed hypoechogenicity and an enlarged thyroid volume. Hashimoto's thyroiditis was diagnosed. Food allergy and infectious diseases were not detected. As an increased level of the tissue transglutaminase was found, celiac disease was assumed.
Method: The boy was treated with levothyroxine 150 µg and a gluten-free diet. The gastrointestinal symptoms improved; however, antihistamine intake up to 4 times per day was needed to control the csU. Therefore, we started monthly therapy with subcutaneous omalizumab 300 µg.
Results: After six injections, the clinical scores improved from 4 to 12 (UCT) and from 28 to 18 (UAS7). After ten injections, the symptoms continued to improve incrementally (UCT remained stable, while UAS7 decreased to 14). No face swelling was seen. However, the administration of antihistamines four times a day was still necessary. In the course, the thyroid gland showed increasing hypotrophy, and levels of TSH clearly increased, whereas the tissue transglutaminase level normalized.
Conclusion: This case is remarkable since the association of csU with autoimmune diseases is rare. It is assumed that about 7% of autoimmune thyroid disease patients and 1.5% of celiac disease patients also suffer from csU. Females seem to be more prone to autoimmune disease. Our patient is a young boy suffering from two different autoimmune diseases in addition to csU. This rare constellation may be the reason for his slow and still incomplete response to therapy.

TP0873 | A case of cold induced anaphylaxis

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Case report: Background: Cold urticaria, a form of physical urticaria, is caused by the release of histamine and other proinflammatory mediators from mast cells after skin contact with cold. Among all physical urticaria, cold urticaria is the second most common urticaria after symptomatic dermographism. The frequency of cold urticaria is estimated to be approximately 0.05%. Cold-induced anaphylaxis in children is very rare and is reported as a case report in the literature. Here we report a case of cold induced anaphylaxis.

Case report: A 16-year-old male patient was admitted to the outpatient clinic with complaints of generalized redness, edema and pruritus on his lips, face, hands and throughout his body and shortness of breath when he had cold exposure. These complaints passed within 2 hours after heating. The ice cube test was applied to the patient and it was rapidly positive within 3 minutes. The patient was diagnosed with cold anaphylaxis. The family was informed about the necessity of not being cold contact. Adrenaline autoinjector and antihistamine were prescribed.

Conclusion: Cold anaphylaxis is a very rare life-threatening condition. An ice cube test, which is a simple test, can be easily performed in patients with complaints after cold exposure. It is very important to diagnose patients, to regulate life conditions and to give appropriate treatment.

TP0874 | Cold urticaria and human parvovirus B19 infection? – A case-report

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Case Report

Background: Cold urticaria is a subtype of physical urticaria characterized by pruritic wheals, angioedema or anaphylaxis triggered by skin contact with cold objects, cold liquids and/or cold air. This is due to cutaneous mast cell activation and release of proinflammatory mediators after cold exposure. The vast majority of cases is idiopathic but up to 5% can be associated with infections (syphilis, borreliosis, measles, varicella, hepatitis, mononucleosis, human immunodeficiency virus). To our knowledge, human parvovirus B19 (HPVB19) infection has not yet been associated with cases of cold urticaria, but with some cases of acute urticaria.

Case Report: We report a case of a 39-year-old woman, referred to our consultation for a sudden episode of generalized pruritic maculopapular exanthema, associated with dyspnea, vomiting and lipothymia, after bathing for about 30 minutes in sea water (14-15°C). The symptoms reverted spontaneously in about 3 hours. A few weeks later she had facial edema after wetting her face with sea water. After that, she tolerated bathing in a swimming pool and having cold drinks.

The patient has a personal history of Graves' Disease diagnosed two years ago, with positivity for anti-thyroid antibodies, that is controlled with Methylbasol therapy.

She performed a TempTest® that was positive from -4°C to 18°C. Cryoglobulin screening was negative. We found a positive IgM antibody against HPVB19 with no symptoms suggestive of a viral infection, three months after the diagnosis. She has a new control HPVB19 serology ongoing at this time. Cytomegalovirus, Epstein-Barr virus, adenovirus, coxsackie and echovirus were IgM negative.

The patient was advised to avoid contact with cold water and she has as needed antihistamines and self-injected adrenaline in case of unexpected contact, with no subsequent episodes at present time.

Conclusion: At this time, we cannot exclude the possibility of immunology mimicry with HPVB19, since the patient had no clinical symptoms associated with the positivity of the IgM serology. The only positive data are the presence of thyroid autoimmunity, although already diagnosed two years ago with no prior symptoms of cold urticaria.

Although cold urticaria is usually considered a benign and self-limiting pathology, an exhaustive complementary study should always be performed in order to exclude some possible associated pathologies that can require another type of specific therapeutic approach.

TP0876 | Melkersson-Rosenthal syndrome presenting as a misdiagnosis of angioedema

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Case report: Background: Diagnosis of angioedema can be a challenge for physicians. Melkersson-Rosenthal syndrome (MRS) – is a rare neuro-mucocutaneous disease of unknown origin, clinically recognized by recurrent angioedema of lips and face, facial palsy, and fissured tongue.

Objective: Our aim was to present the case of delayed diagnosis of MRS after two decades of clinical symptoms.

Methods: 57-year-old Caucasian male patient was complaining of recurrent swelling of lips lasting for few days and resistant to antihistamines. Attacks of facial angioedema without urticaria started 20 years ago, infections, allergy, autoimmune diseases, hereditary angioedema were excluded. During the period of 20 years, the patient had recurrent episodes of tingling and tension of the

lips followed by swelling of the lower part of the face, sometimes provoked by labial Herpes simplex infection. The swelling of the face usually resolved after intake of oral prednisolone, later on the asymmetric face was visible between attacks. MRS was suspected as angioedema was combined with left facial nerve palsy and fissured tongue. Patient's mother also had a fissured tongue but no angioedema history. Lower lip biopsy and histology revealed nonspecific, inflammatory changes, infiltration of immune cells and telangiectasia and no specific changes like cheilitis granulomatosa were found.

Results: Facial angioedema resistant to antihistamines was one of Melkersson-Rosenthal syndrome combined with facial palsy, fissured tongue and positive family history of partial MRS.

Conclusion: Angioedema is the main symptom of MRS associated with facial palsy, and fissured tongue. Patients with angioedema should be evaluated for concomitant symptoms and family history of rare syndromes such as MRS especially in treatment resistant cases.

SUNDAY, 2 JUNE 2019
TPS 15
CASE REPORTS IN FOOD ALLERGY I

TP0877 | A case with acute baked milk protein-induced enterocolitis syndrome

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Case Report:

Introduction: Acute food protein-induced enterocolitis syndrome (FPIES) is a non-IgE mediated food allergy (FA). Of the two clinical phenotypes, acute FPIES develops when the offending food is ingested intermittently or after a period of avoidance. Knowledge in baked-food tolerance which is well-known in IgE-mediated FA is limited in FPIES. This report presented an extremely reactive infant with acute FPIES.

Case report: An infant with atopic dermatitis had started to have blood tinged stools at 2 months of age. All cow's milk (CM) containing foods were eliminated from infant's and nursing mother's diet. At 4.5-month of age, after feeding with 2 tea spoons of yoghurt for the first time, he vomited 4 times, became lethargic but had no urticaria or any other symptoms. The infant was treated with intravenous fluids and internalized for five days. Milk and egg white specific (s) IgE were < 0.35 and 0.87 kU/L, respectively. At 6 months of age, when an oral challenge test (OCT) with infant formula containing CM protein was performed, repetitive vomiting, lethargy and diarrhea was observed. CM, egg, chicken and cow's meat were also eliminated from the infant's diet. At the first admission to our hospital at 8.5 months of age, egg yolk, egg white and CM sIgE were 0.22, 2.22 and 0 kU/L, respectively. There was no reaction in OCT with red meat, baked egg yolk and white. At 20 months, an OCT with baked milk (cake) was performed and totally 0.175 gram cow's milk protein was given. No reaction was observed within 4 hours of the OCT. However, recurrent vomiting with cough and lethargy developed 4 hours later. Symptoms resolved with intramuscular adrenaline, intravenous fluids, methyl prednisolone and ondansetron treatments at the hospital. Currently, the infant is 26 month-old and has been ingesting boiled whole egg without symptoms but cannot consume any food containing CM.

Conclusion and discussion: There has been no laboratory test evaluating the severity of FPIES. Knowledge about tolerance to heat-modified food in FPIES has limited. It is therefore recommended that OFC test should be performed under close supervision with longer observation period for at least 4 to 6 hours.

TP0878 | Two Cases Of Allergy To Lupin In Vegan Ice-Cream

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Case report:

Background: Lupin is considered a 'hidden food allergen' as small amounts can be present mixed in many foods, mainly with wheat flour. Since its introduction in Europe in 1990s there have been increasing reports of isolated lupin allergy with severe allergic reactions. Lupin is known to cross-react with other members of the legume family. Our case reports describe 2 patients with no previous history of food allergy, who presented with severe allergic reactions/anaphylaxis after having vegan ice cream containing lupin and were subsequently diagnosed with lupin allergy.

Cases: Patient A: 53-year-old male who had eaten vegan ice cream and about 15-30 minutes later, his eyes felt prickly, he developed lip swelling and abdominal pain. He tried to go to sleep but was feeling drowsy, his throat was prickly and he felt wheezy. He awoke feeling hot, sweaty and itchy with a red rash in his axillae. He went back to sleep and his symptoms had all resolved in the morning. He noticed that the ice cream that he had eaten contained lupin and no other obvious culprit. Skin prick tests were positive to lupin.

Patient B: 47 year-old-female who, immediately after having vegan ice cream, felt as if her tongue and mouth were swelling and had difficulty breathing. She took 20 mg of cetirizine, steroid tablets, which she had for her asthma, and her salbutamol inhaler. Symptoms settled in 1-2 hours. She reported an asthma attack 10 years before, 3 hours after eating a vegetarian burger; this was attributed to nut allergy and she has since avoided nuts. No culprits were identified for the 2nd episode. Skin prick tests were positive to lupin flour; negative to soya, peanut and all tree nuts.

We established that the vegan ice-cream that both patients had eaten contained lupin flour, as declared on the ingredients list. Patients were advised to avoid all products containing lupin, given an anaphylaxis action plan and were prescribed 2 adrenaline auto-injectors.

Conclusion:: Lupin (flour) has been reported to be added to bread, pasta, breadcrumbs, buns, biscuits, pancakes, muffins, croissants, chocolate, brownies, waffles, sauces, milk or soya substitutes, in foods for coeliac patients, chicken broth cubes, and dehydrated chicken soup. However, we are reporting these cases as we felt that ice cream is an unusual product to contain lupin, and indeed has not been reported to our knowledge, hence our aim is to increase awareness of this possibility.

TP0879 | Anaphylaxis due to allergy to coconut

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Case report: Introduction: Allergy to coconut is a rare pathology and there are very few cases described in the literature. We present a case of a 17 years old female that presented respiratory distress, dysphagia, general urticaria five minutes after eating a coconut cake, five years before coming to our outpatient clinic. She also refers to presenting urticaria after taking a soaps containing coconut derivatives about two years ago. She does not have any problem with other foods and usually consume nuts. She has not eaten more coconut despite not avoiding it.

Materials and Methods: For the diagnosis of allergy intracutaneous tests have been carried out against a battery of foods, including nuts, lentil and coconut, and epicutaneous tests against cosmetics and dermoemulsant vehicles, including those derived from coconut. In addition, analytical test have been carried out on the detection of food IgE (nuts, lentil, wheat, soy and coconut) and basophil activation test against water and coconut milk. Study of the molecular mass of specific IgE-binding proteins using SDS-PAGE immunoblotting method according to Lammli in two electrophoresis conditions.

Results: - Prick test: coconut pulp 6 mm, coconut milk (82% pulp coconut) 5 mm, coconut water (100% coconut) 3 mm. Histamine control 1% 5 mm and with 10 negative controls of the prick in fresh.

- Epicutaneous tests against cosmetics and dermoemulsant vehicles (including 21 contactors): negatives with reading at 48, 72 and 96 hours.

- Coconut IgE < 0.1 Uk/L. The rest of IgE detected against food presented values < 0.1 Uk/L.

- Basophil activation test: positive 15% with coconut milk (82% pulp coconut) and negative with coconut water (100% coconut). Greater than 5% is considered a positive result, in this case allergy is confirmed.

- SDS-PAGE immunoblotting: coconut water extract: 70 kDa, 55 kDa, 50 kDa, 40 kDa, 37 kDa and 18 kDa. Coconut milk extract: 45 kDa and diffuse fixation between high molecular masses. Coconut pulp extract: 60 kDa, 50 kDa and 39 kDa.

Conclusion: In summary, we report a case of anaphylaxis after coconut intake presenting in a 17 years old women. Due to the increasing use of coconut and its derivatives in industry, the allergenic capacity of different coconut proteins should be studied in greater depth.

TP0880 | Case report: Goat's milk anaphylaxis in a cow's milk tolerant child

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Case report: Goat's milk (GM) allergy commonly occurs in patients with cow's milk (CM) allergy due to high degree of sequence homology between the milk proteins. It is unusual for patients to have isolated GM allergy. The literature on GM allergy in CM tolerant patients is limited to case reports and case series, mostly originating from Europe.

We present a unique case of an Asian child who is tolerant of CM but experienced anaphylaxis to GM formula. The patient's parent gave written informed consent for publication of data.

Patient H is a 7 year old Chinese boy with background of eczema, allergic rhinitis and shellfish allergy. He tolerates daily CM ingestion. He first encountered GM at 6 years of age when he ate GM powder sweets. Thirty minutes after ingestion, he experienced urticaria, cough and wheeze. He visited his family doctor and was treated with oral anti-histamines and nebulized bronchodilators.

At 7 years of age, he drank 70 mL of GM formula. Within 15 minutes, he developed anaphylaxis, with angioedema, hoarseness of voice, breathlessness, vomiting, abdominal pain and drowsiness. He visited the emergency department and was treated with one dose of intramuscular adrenaline. Serum tryptase was elevated at 14.6 ug/L, 2 hours post-reaction.

On further evaluation, prick-to-prick fresh goat milk was 12 mm, goat milk formula 7.5 mm and diluent 0 mm. Specific IgE cow milk 0.83 kU/L, goat milk 54.8 kU/L, nBos d8 casein 1.51 kU/L. His baseline tryptase is 2.4 ug/L.

He has been advised dietary avoidance of goat milk and sheep milk.

Discussion: The Bovidae are a mammalian, ruminant family that comprises of subfamily bovinae (cow) and caprinae (goat and sheep). In 2006, a case series from France described 28 children tolerant of CM but clinically reactive upon ingestion of goat's and sheep milk (GSM) products, namely cheese. Despite amino acid sequence homology of 85-90% between CM and GSM casein, analysis of IgE profile from these patients revealed a high recognition of GSM calcium-binding caseins and poor recognition of CM caseins.

In Asia, the main source of milk is cow. Since 1990, powder goat milk formulated with 40-60% GM solids has been introduced and gaining popularity among infants and children in the Asia-Pacific region. Given the global rise of allergic diseases, our case report highlights a unique cause of food anaphylaxis that may be more apparent with increasing consumption of GM in Asia.

TP0881 | MOLD—Triggered anaphylaxis

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Case Report:

Background: Mold sensitization usually brings on respiratory symptoms such as rhinoconjunctivitis and asthma. Reactions due to mold ingestion have seldom been described. Penicillium is the predominant mold in short-time curated pork meat. The intake of these products, typical in Spanish cuisine, can develop allergic reactions.

Method: A 13 years old female, immediately after eating a pancake and some appetizers, presents hives, angioedema, dry cough, wheezed dyspnea and dizziness, needing urgent adrenalin treatment in emergency services. She also presents these symptoms when eating various curated pork products (fuet, salchichon). She has rhinoconjunctivitis and dyspnea in spring and autumn. She had overcome an egg and milk allergy.

Results: Skin prick test was positive to *A. alternata*, olive, grass pollen and barley. The prick-prick test was positive to both skin and meat of the fuet. The specific IgE was positive to several molds (A. *alternata*, *A. fumigatus*, *C. herbarum*, *P. notatum*).

Patient's IgE recognized some proteins in the extract of the fuet peel, with a molecular weight between 50 and 75 KDa, that could be related to *P. notatum*. Additionally, the extract of *P. notatum* inhibited the proteins of fuet according to the Western Blot-inhibition test carried out. Oral challenge tests with the pancake and the appetizer involved were done, both being tolerated without issues. The patient was diagnosed of anaphylaxis due to *P. notatum* hypersensitivity.

Conclusion: The association between mold allergy and asthma due to environmental exposure is well known; however, there are few published articles that relate the intake of foods that may contain molds and the development of anaphylaxis. We hereby introduce a case of a patient with mold sensitization that shows episodes of anaphylaxis both by inhalation of spores and by ingestion of foods that may contain P*enicillium*.

TP0882 | Cow's milk allergy – A hidden diagnosis of late presentation

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Case Report:

Background: Cow's Milk Protein Allergy (CMPA) is the most frequent food allergy in the first years of life and is usually transient. Cow's milk contains 2 types of proteins: caseins, the most frequent in percentage and with the highest allergenic potential, and whey proteins, the most common being β-lactoglobulin and α-lactalbumin. The allergic process may be IgE-mediated or non IgE-mediated: the first, most frequent, can cause symptoms up to two hours: urticaria, angioedema, vomiting, diarrhea or even anaphylaxis; the second, more than two hours after exposure, can cause symptoms such as atopic dermatitis, eosinophilic esophagitis or enterocolitis.

Case Report: Woman, 59 years old, healthy, with no history of previous food allergic reaction. She went to the emergency department due to a clinical presentation of lip edema and generalized pruritic rash fifteen minutes after ingesting a coconut delight pie made of condensed milk, cow's milk, coconut milk and grated coconut, without severity factors or associated cofactors. She had a new episode with similar symptomatology about one month later, fifteen minutes after ingesting a yogurt of piña colada composed of milk, coconut and pineapple. Twelve years earlier she had a skin reaction which she couldn't characterize and performed skin prick tests (SPT) positive for casein, avoiding cow's milk until now. She is a patient who has not been breastfed and cow's milk has been introduced early in its food diversification, with no reported complaints until now. During the investigation at the consultation she performed skin prick tests with natural foods that were positive for the coconut delight pie and the yogurt of piña colada that were involved in the reactions, as well as for cow's milk extract, caseins and β-lactoglobulin, and negative for the coconut extract and cream.

Conclusion: CMPA is, in most cases, a transitory condition limited to childhood. Based on a high pretest probability and with positive skin tests, the diagnosis of late CMPA can be confirmed, rather than a coconut allergy as initially suspected, although the clinical presentation is not the most common and compatible with the natural history of this allergy since the symptoms started later in life. The patient is currently being followed up at the consultation to continue the investigation and subsequent appropriate treatment, and should avoid, for soon as now, not only cow's milk, but also goat and sheep because of possible cross-reactivity.

TP0883 | A case of eosinophilic gastroenteritis caused by milk allergy in neonate with sepsis

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Case Report: GI allergy is thought to be cell mediated or mixed IgE and cell mediated disease. Of GI allergy, eosinophilic gastroenteritis (EGE) is a rare, heterogeneous disorder characterized by gastrointestinal (GI) symptoms and eosinophilic infiltration in the GI tract. The clinical manifestations of EGE vary depending on the site of the affected GI tract and the depth of involvement, and include abdominal

pain, nausea, vomiting, diarrhea, or bloating. The clinical management of EGE is difficult owing to its enigmatic nature and unknown etiology. Currently, it is not easy to differentiate patients with EGE who need long-term or repeated therapy from those who may have a transient illness without relapse. Dietary elimination is reported to be effective in some patients with EoGE, which indicates that this condition, like EoE, is related to an allergic disorder. Moreover, most reports on EGE are case report based owing to its rarity; therefore, an overview of this disease is difficult to comprehend. Here, we attempted to identify the best strategy for the management of adult EGE by analyzing its clinical course and response to treatment.

A 5 days old milk formula male infant presented with high fever and bloody diarrhoea of 4 days and stool frequency of 10 times per day. There was fever, vomiting or abdominal distension. Both parents have allergic rhinitis. Lab investigations done included Cell Blood Count (CBC) and abdominal ultrasound both of which were abnormal. Stool testing showed red blood cells. According to allergy test, the boy had positive allergen to milk (5.11 kUA/l).

A diagnosis of eosinophil gastroenteritis was made by sigmoidoscopy and result of biopsy that Increased number of eosinophils in lamina propria (up to 90/HPF) with intraepithelial eosinophils: up to 10/HPF. After antibiotic medication and restriction to milk for 5 days, following the abdominal ultrasound was normal. Intravenous cefuroxime and metronidazole were given for 10 days without resolution of bloody stool. The case was reviewed, and it was noted that, the high fever, vomiting and abdominal distension in neonate support the diagnosis of eosinophil gastroenteritis, not sepsis caused by infection. Maternal dairy elimination to milk was continued for 6 months for breast milk feeding. After 6 months later, the boy had negative allergen to milk (0 kUA/l) and started milk formula again but no diarrhea, vomiting, and fever.

TP0884 | Cat-Pork syndrome as cause of anaphylactic reaction to well cooked meat

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Case report: Cat-pork syndrome is rare, occurs in patients allergic to cat dander (CD) and is caused by cross-reactivity (CR) between serum albumin (SA) of cat and pork. Usually there is respiratory allergy to CD that precedes alimentary allergy. This suggests a primary sensitization to cat SA. Since SA is thermolabile, the reaction tends to be more severe when the meat is less cooked. CR with others mammalian SA may occur.

Woman, 27 years (y), from Mozambique, living in Lisbon since 2010. She has rhinoconjunctivitis that has been worsening in the past 3 years. She always had dogs and cats in outdoor; and got a dog and a cat that live indoor, 6 and 3 years ago, respectively. In the last 8 years she has been eating mammalian meat and had reproducible local oedema when contacting with raw pork meat (PM). She also had 2 systemic mucocutaneous reactions 30 minutes after intake of small amounts of pork meat in the last 6 years. Skin prick and prick-prick tests were positive for extracts from *Blomia tropicalis* (BT), *Acarus siro* (AS), olive pollen (OL), grass pollen (GR), CD, dog dander (DD) and raw PM; it was negative with cooked PM. She developed an erythematous and pruriginous papule 5 minutes after contact with raw PM on skin, compatible with an immediate reaction. Specific IgE were positive for CD, PM, BT, AS, OL and GR and the microarray ISAC showed sensitization to several allergens, including Fel d 2. Two oral provocation tests (OPT) with well-cooked meat were positive, developing anaphylaxis after had eating 2 and 8 g of well-cooked PM and cow meat (CM), respectively. SDS PAGE IgE immunoblotting assays were performed with pork meat extract, and a 60 kDa band was detected. In the Immunoblotting-inhibition assays, cat SA produced a total IgE binding inhibition to pork meat extract, which proves CR between the two SA, hence confirming the cat-pork syndrome diagnosis. The inhibition assays with other mammalian meats are in progress. An epinephrine autoinjector was provided, although a mammalian meat free diet was advised.

A cat-pork syndrome diagnosis was made with probable clinical CR to other mammalian SA. It was not expected neither the severity nor the reaction to the well-cooked meats.

This case should raise awareness for performing OPT with well-cooked mammalian meats in patients with cat-pork syndrome in order to stablish tolerance threshold and avoid possible anaphylactic reactions. It would be interesting to study the effect of immunotherapy for SA cat allergy on food allergy.

TP0885 | Two adult cases of jellyfish food allergy

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Case report: We had the opportunities of diagnosis of anaphylaxis caused by jelly fish food allergy. Case 1 A 35-year-old woman. She had been frequently stung by several kinds of marine creatures including jelly fish. Anaphylaxis occurred immediately after ingesting cold antipasto of jellyfish at a Chinese restaurant. Total IgE value in serum was 545 IU/mL. CAP-FEIA showed sensitization to mites and some sea foods. Case 2 A 35 - year - old woman. She had been stung by jelly fish during snorkeling. She had experienced twice anaphylaxis which occurred immediately after ingesting home-maid antipasto of jellyfish. Total IgE value in serum was 587 IU/mL. She was sensitized to mites and *Anisakis simplex*. Intriguingly, main manifestations of anaphylaxis in both cases were gastrointestinal symptoms;

nausea, vomiting, abdominal pain, accompanied by hives. Also, both of them loved to swim in the sea and had been stung by marine creatures. These clinical features were consistent with previous reports of jelly fish allergy. Basophil activation test using patients' peripheral whole blood showed jelly fish components lead CD203 expression on the surface of basophils in these two cases. Examinations using sodium dodecyl sulfate poly acrylamide gel electrophoresis and immunoblotting showed that acid-soluble collagen fraction from jellyfish contained above 250 kDa weighed protein was supposed to cause anaphylaxis in our cases. Although past reports showed some cases with jelly fish food allergy were associated with poly glutamine acid which contained inside the sticky substance clinging around natto beans, but our cases did not show any sensitization to such allergen.

TP0886 | Anaphylactic shock to anemones (actinia equine) intake

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Case report: Anemones are coelenterates animals, responsible for more poisoning than any other marine phylum. Systemic reactions are rare and reactions to venom are presumed to be toxic rather than allergic. A 15-year-old male patient with family history but no personal history of allergy. Five minutes after having eaten two cooked anemones (Actinia equine) in a restaurant, he started to have severe abdominal pain, followed by otic pruritus, which turned into generalized urticaria and evident facial angioedema. Later he suffered from aqueous rhinorrhea, nasal blockage, dyspnea and dizziness. He was admitted at the Emergency Unit of a Primary care centre, showing mild arterial hypotension. He had to be given parenteral drugs and 6 h later, the patient was discharged after complete resolution of clinical manifestations. The patient had previously eaten cooked anemones, having no symptoms.

Skin prick test (SPT) performed with commercial extracts were positive to house dust mites (HDM), and negative to other common inhalants, foods, and Anisakis simple. Prick-to-prick with the raw implicated anemone (Ac. equine) was strongly positive in patient (two control were positive < histamine, because it is irritant). Prick-to-prick with the cooked anemone (Ac. equine) was positive in patient (two control were negative).

ImmunoCAP ISAC (Thermo®) was performed, showing a single sensitization to Der p 1 and Der f 1, house dust mites allergens. Sodium dodecyl sulphate polyacrylamide gel electrophoresis (SDS-PAGE) was performed to raw and cooked anemones, showing low bands in both: raw and cooked.

SDS-PAGE immunoblotting experiments using the patient's serum revealed four different immunoglobulin (Ig)E-binding protein bands of 37 kDa, 40 kDa, 50 kDa and 100 kDa in raw anemone extract. The 37 kDa protein could be a tropomyosin.

In conclusion, this case illustrates IgE-mediated anaphylactic shock to Ac. Equine, a type of anemone. Although contact allergy to anemones had been described before, food allergy to anemones has not been previously reported in humans. Even though one of the proteins involved could be a tropomyosin, given the fact that the patient did not show a sensitization to Der p 10 (HDM tropomyosin), anemone allergy could not be leaded by a primary sensitization to HDM.

TP0887 | Clinical case of urticaria, accompanied by multiple cross sensitization to pan-allergen tropomyosin, confirmed with multiplex allergy test ALEX

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Case report: A 46-year-old woman complained of urticaria, facial erythema, and pharyngeal itching after consumption of salad containing seafood.

Anamnesis of the disease: she considers herself to be ill for about 20 years, when nasal congestion, periodical profuse mucous discharge from the nose, and sneezing appeared. Symptoms appear all year round with temporary effect after intake of antihistamines. Intensive skin itching, severe urticaria, swelling of the lips, nausea, and dizziness appeared for the first time approximately 5 years ago after consumption of oysters, wine and strawberries. Within the last five years, the aforementioned complaints recurred in six cases. The woman consumes shellfish and fish from time to time and avoids oysters. Manifested local allergic reaction to gnats' bites (swelling, redness, itching) is observed.

Past medical history. The patient was born in Kyiv. At 26, she moved to Japan for permanent residency. She lives on the first floor, near the ocean. Pets – a cat, a dog. Prefers Mediterranean and Japanese cuisine (in particular, sushi with raw fish).

Objectively: The skin and visible mucosa are pale rosy; individual bright rosy urticarial rashes are observed on the skin of the upper arms and forearms, cheeks are of bright rosy colour. Nasal breathing is slightly difficult.

Component diagnosis: genuine sensitization to epidermal allergen of house dust mites sIgE Der p 10 (Tropomyosin) 9.96 kU/l, cross-sensitization to tropomyosin Anisakis simplex sIgE Ani s 3 (Tropomyosin) 1.86 kU/l, American cockroach sIgE Per a7 (Tropomyosin) 0.39 kU/l, crab 35.13 kU/l, lobster 0.40 kU/l, squid

0.77 kU/l, oysters 1.55 kU/l, shrimps 0.45 kU/l. Sensitization to epidermal cat allergen Fel d 12.38 kU/l.

Diagnosis: Chronic urticaria. Food allergy to seafood. Multiple cross-sensitization to pan-allergen tropomyosin. Chronic allergic rhinitis.

Recommended: sanitization of the household, excluding contact with the cat, avoidance of seafood.

TP0888 | First characterization of allergens causative of occupational asthma by lathyrus sativus flour

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Case Report:

Background: Grass pea or vetchling (*Lathyrus sativus*) is a legume belonging to the *Fabaceae* family. Up to now, three cases of occupational asthma related to *Lathyrus sativus* flour (LSF) have been published but the proteins responsible for occupational asthma by LSF had never been characterized before.

Case report: We report the case of a 34 year-old female non-smoker who reported a 2 year history of nasal pruritus, rhinorrhea and cough related to her work environment in a market of bulk legumes, flours and spices. She reported worsening symptoms specially when removing LSF, which she consumed it cooked with good tolerance.

Methods: Skin prick test with battery of inhalant allergens, foods and panallergens and specific IgE to nuts, LTP's and profilin were performed. Fractional exhaled nitric oxide (FeNO), basal spirometry, bronchodilation test, bronchial challenge test with methacholine (BCTM) and specific bronchial challenge test (SBCT). Protein extract from LSF. SDS-page, Immunoblotting and molecular characterization of IgE binding bands by mass spectrometry.

Results: Prick test was positive to for LSF, cumin, oregano, fennel, peppermint, garlic, tomato, and LTP. Specific IgE was positive to nut: 1.06 kU/L, hazelnut: 3.17 kU/L, pistachio: 0.53 kU/L, pipe: 2.00 kU/L, peach: 2.57 kU/L, peanut: 0.62 kU/L, LTPs (rPru p 3: 9.56 kU/L, rCor a 8: 5.58 kU/L, r Ara h 9: 3.48 kU/L); and negative to grass pea (0.17 kU/L), chestnut and profilin. FeNO was 77 ppb. Baseline spirometry's values were normal and bronchodilation test was negative. BCTM performed while the patient was working revealed bronchial hyperreactivity (PC_{20} 0.93 mg/mL). SBCT with handling LSF elicited an immediate clinical and spirometrical response. Twenty four hours after the SBCT, the BCTM worsened (PC_{20} 0.29 mg/mL) and FeNO elevated up to 85 ppb. SDS-page and Immunoblotting detected binding IgE band with molecular weight about 25, 37 and 50 kDa which were identified by mass spectrometry as was identified as a conviciline (50 kDa) of the genus *Lathyrus*, a legumine from *Pisum sativum* (37 kDa) and a "seed albumin" of *Lathyrus sativus* (25 kDa).

Conclusion: We report the first characterization of allergens in occupational asthma with LSF, demonstrating SBCT positive and *in vitro* study with specific IgE determination to three different proteins with an approximate molecular weight of 25, 37 and 50 kDa.

TP0889 | Anaphylaxis induced by baker's yeast allergy—A case report

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Case report: Sensitization to fungal allergens is common in respiratory and cutaneous diseases. However, systemic reactions following ingestion are rare. The authors describe a case of a 42-year-old women sent to our Allergy and Clinical Immunology consultation (ACIC) due to recurrent anaphylaxis. In November 2016 she began to experience daily symptoms characterized by nausea, abdominal distension, colic abdominal pain and constipation, which she associated to the ingestion of bread. In November 2016 she was admitted to our emergency department and was hospitalized with an episode of anaphylaxis, one hour after eating wheat bread and chicken soup with egg. In February 2017, against medical indication, she reintroduced wheat bread and developed urticaria in the upper limbs and anterior trunk associated to abdominal pain. One week later, against medical recommendations, she reintroduced wheat bread and developed an anaphylactic shock minutes after the ingestion and was hospitalized. Diagnostic workup, 8 weeks after first episode of anaphylaxis, started by skin prick tests (SPT) and blood specific-IgE, which was negative for flours, milk, and egg allergens. Prick-to-prick tests (PTP) for cooked and raw egg, milk and flours (wheat, corn, rice, rye and barley) were all negative. Serum basal tryptase was 3.5 µg/L and 29.4 µg/L measured 1 hour after the first episode of anaphylaxis. Due to the fact that all suspected allergens were negative in SPT, PTP and IgEs, we started by performing an oral food challenge (OFC) to milk, which was negative. Afterwards, she was submitted to an OFC with muffin (20 g of wheat flour with baker's yeast, egg, sugar and 3 g of cow's milk) and 5 minutes after a cumulative dose of 10 g she developed palmar erythema and pruritus, nausea and abdominal pain. SPTs and PTP to flours were repeated several times with negative results. PTP test to baker's yeast was positive (papule of 15 × 11 mm). PTP test to baker's yeast was performed in 4 atopic controls with negative results. We suggested an OFC with muffin without baker's yeast, which the patient refused. For better understanding of this case, we requested an immunoblotting, which results are not yet available. This patient follows a diet without flours for about a year, being asymptomatic since then. These results suggest a systemic and severe hypersensitivity to baker's yeast. According to

the literature to our knowledge this is the first case report describing anaphylaxis to baker's yeast.

TP0890 | Oral allergy syndrome—A case report

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Case report: Background: Oral Allergy Syndrome (OAS) is an allergic reaction that mainly occurs after oral contact with raw fruits, vegetables or nuts. It can be caused by cross-reactivity between birch pollen allergens (Bet v 1) and food proteins. The PR-10 proteins are the most important family of PR proteins associated with OAS. Bet v 1 is a PR – 10 protein, and is the major allergen in birch pollen, being highly similar to other PR-10 proteins in plant food such as *Rosaceae* fruits. Generally, symptoms associated to OAS are mild, limited to the oropharynx, although, systemic reactions may occur. Characteristically, after cooking, tree-pollen associated foods are well tolerated.

Case Report: We report a case of a 47-year-old man with symptoms of oral-pharyngeal pruritus and odynophagia immediately after eating apple, pear, grapes, peach, cherry and prune (with and without peel). He tolerated orange, tomato, banana, pineapple and dry fruits, including nuts. Skin prick tests were performed with the fruits from which he complained about, with profilin and with lipid transfer protein (LTP) and they were all negative; skin prick tests "european standard" series were positive to *phleum*, olive tree and grass. The prick-prick tests to apple, pear, grape and prune were all positive (peach was unavailable). We performed ISAC® test which revealed sensitization to PR-10 proteins, including mainly Bet v 1 (birch pollen), Cor a 1 (hazelnut), Mal d 1 (apple), Pru p 1 (peach) and Act d 8 (kiwi); to Grass group 1 (Phl p 1) and to Mite (Der f 1 and Der p 1). Currently, he's under eviction of these fruits when raw and remains asymptomatic. He tolerates them when they are cooked.

Discussion: OAS more frequently occurs with profilin, rather than with PR-10 proteins. The primary treatment of OAS is avoidance of food triggers. Because digestive enzymes in gastrointestinal tract readily breakdown food allergens related to PR-10, symptoms are limited to the oropharynx. Allergens are typically labile and therefore heat sensitive, so that patients tolerate cooked food. Pollen immunotherapy may be considered; however, more prospective studies are needed.

TP0891 | Scarlet shrimp: Several allergens identified

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Case report: Shellfish allergy is one of the most prevalent food allergies in several countries and its prevalence has risen in recent years. Several major and minor allergens have been identified and their genes cloned. A scarlet shrimp *(Aristaeopsis edwardsiana)* is a crustacean with similar appearance of prawn or shrimp but quite bigger and tastier, frequently consumed in Mediterranean countries

Case: A 68 years old woman with history of hypertension and diabetes, had an anaphylactic reaction some minutes after eating some scarlet shrimps. She suffered skin and throat stinging, breathlessness (saturation 88%), fatigue and low blood pressure (75/43) that required medical attention with antihistamine, corticoid, two doses of adrenalin and intravenous saline drip.

Prick by prick was positive with scarlet shrimp and prawn. Serum tryptase was negative (8.21 μg/l)

SDS-PAGE immunoblotting was carried out with patient serum and scarlet shrimp abdomen and cephalothorax extracts

IgE binding bands of aprox. 96, 66, 55, 50, 39, 31 and 28 kDa were detected. Shellfish IgE binding proteins with similar molecular masses have been described: triose phosphate isomerase (28 kDa), arginine kinase (40 kDa), enolase (47 kDa), pyruvate kinase (64 kDa).

Discussion: Among crustaceans, shrimp is the most predominant cause of allergic reactions and thus it is extensively studied. However, the whole spectrum of shrimp allergens is unknown and few of them have been completely characterized.

TP0892 | A case of allergic glossitis caused by fish, crustacea, and mollusca

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Case report: We report the case of a 3-year-old girl who had no food allergy including that of fishes, crustaceans, and molluscs, and no other allergies such as asthma and atopic dermatitis. After consuming fish, crustaceans, and mollusks such as tuna, shrimp, squid etc. one year ago, redness and pain appeared on her tongue within several hours to a day, and she subsequently became averse to consuming meals. There were no symptoms other than glossitis; no gastrointestinal symptoms such as abdominal pain and diarrhea and

skin symptoms such as urticaria were noted, and there was no onset of dermatitis even if fishes, crustaceans, and molluscs had been touched by hand.

In blood tests, specific IgE antibodies against tuna, shrimp, and squid, which complained of symptoms, were all negative. Due to suspected delayed-type allergic reactions, a skin patch test for allergy of tuna, shrimp, crab, laver, and petrolatum was conducted, and the results were positive for tuna, shrimp, and crab.

Diagnosis of glossitis due to Type IV allergy to fish, crustaceans, and molluscs were confirmed, based on the fact that ingestion of tuna, shrimp and crab necessarily resulted in glossitis, and since glossitis was not noted unless she consumed these items, as well as based on the results of skin patch test.

Glossitis due to allergic mechanisms is mostly caused by dental metals, while a few reports on glossitis caused by food have been reported. We report such a case here, and have discussed the relevant literature.

TP0893 | A first case of LTP syndrome in Japan

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Case report:

Background: Lipid transfer proteins (LTP) syndrome is known as one of the most common causes of plant food allergy, especially in Mediterranean countries. On the other hand, no cases about LTP syndrome has been reported in Japan.

Case report: A 28-year-old Japanese female presented syncope, generalized urticaria and lowering blood pressure 15 minutes after a meal of lettuce, avocado, alfalfa, yogurt, and bread. She also had a history of oral allergy syndrome after consumption of apple, peach, soy products. Serum specific IgE levels were positive to Cedar(10.4 Ua/mL), apple(31.8 Ua/mL) and peach(10.3 UA/mL). A skin prick test showed positive for mung bean sprouts, pea sprouts, and tomato. The ImmunoCAP ISAC microarray (Thermofisher Phadia) was also performed. LTP of peach, hazelnut, peanut, platan, and mugwort were positive.

Conclusion: LTP syndrome should be considered also in Japan in case of sensitization to various kinds of fruits and vegetables is suspected. In addition, this case implies the possible cross-reactivity between LTP and sprouts.

TP0894 | Quinoa allergy: A hidden allergen

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Case report:

Background: Quinoa (pronounced "keen-wa") has been cultivated in the Andean highlands since 3000 BC. Its small, very nutritious seeds resemble millet and are very versatile in cooking. *Chenopodium* plants have characteristic leaves shaped like a goose foot. (The genus also includes a common weed, Goosefoot or Lamb's quarters.) Quinoa is a small seed that in size, shape, and colour looks like a cross between Sesame seed and Millet. It is usually a pale yellow colour, but species vary from almost white through pink, orange, red, purple and black. Quinoa is not a true cereal grain but is technically a fruit of the *Chenopodioideae* subfamily. It rarely produces allergic reactions in sensitised individuals.

Case report: 24 year old atopic man presented with history of reaction to a meal containing meat balls and chicken tikka (creamy mild sauce cooked with almonds, coconut and herbs). The patient has developed immediate symptoms which included tingling and swelling of his lip which then progressed to tongue swelling, difficulty breathing, abdominal cramps, vomiting, tingling, blotchy skin rash, sweating and shaking. He improved with antihistamines and steroids. Skin prick and blood tests confirmed sensitisation to peanuts. Patient was advised to get ingredients of the meal as peanut was not known to be present in the meal. Quinoa was one of the ingredients and further investigations confirmed sensitisation to quinoa.

Discussion: Quinoa is a versatile ingredient, and it features in various dishes, ranging from staple foods to spicy delicacies. Quinoa flour, ground from whole seeds, has a delicate, nutty flavour. Allergens have not been characterised. There are 2 case reports of allergic reactions to Quinoa. It remains an uncommon and hidden allergen so far.

Conclusions: Quinoa allergy is a rare food allergy to be aware of. This is important especially when Quinoa could be a hidden ingredient in, commonly used food. We recommend that quinoa allergy worth excluding especially when detail information of meals' ingredients is not fully explored.

TP0895 | Allergy to berries – two unusual cases

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Background: Allergies to berries are very rare. Few cases have been published, mostly reporting anaphylaxis due to sensitization

to specific lipid transfer proteins (LTPs). While LTP sensitization is commonly linked to severe anaphylaxis, sensitization to the pathogenesis-related proteins of class 10 (PR-10) is typically associated with milder symptoms, with the major birch pollen allergen Bet v1 being an important PR-10 representative. We present 2 cases of anaphylaxis to berries that call into question the classical association of LTP versus PR-10 sensitization with the severity of anaphylaxis.

Method: We performed a thorough history, skin prick test with fresh berries and serology in 2 patients.

Results: A 19-year-old atopic Swiss patient developed generalized urticaria, abdominal cramps, dyspnea and loss of consciousness 30 min after consuming raspberries. Upon administration of i.m. adrenaline, i.v. corticosteroids and antihistamines, he fully recovered. Skin prick test with fresh raspberries revealed specific sensitization to raspberries. Laboratory findings showed high total IgE (2680 IU/mL), normal tryptase levels and sIgE to raspberries (> 100 kUA/l). Molecular allergy diagnostics demonstrated strong sensitization to Pru p3 (LTP) and less to PR-10 proteins. A 43-year-old atopic patient from the Mediterranea presented with rhinoconjunctivitis and severe dyspnea immediately after eating fresh mulberries. Treatment with emergency medicines let to full recovery. Skin prick test with fresh mulberries was positive. Total IgE and tryptase levels were normal. Molecular allergy diagnostics showed sensitization to Bet v1 and other PR-10 proteins. No LTP sensitization has been found.

Conclusion: In the patient with anaphylaxis °IV to raspberry, we detected sensitization to LTP and PR-10 proteins, the patient with anaphylaxis °III to mulberry showed sensitization to PR-10 proteins only. A LTP allergen, Rub i3, has been identified in raspberries. Although we were unable to test for Rub i3 in our patient, we presume the strong LTP-sensitization to be responsible for the anaphylaxis. This is unusual in a patient not originating from the Mediterranea. In mulberries, Mor a1 has recently been identified as a PR-10 protein. Thus, we assume a PR-10-related pathomechanism in this patient, being the 2nd report on PR-10-related mulberry allergy. Our cases demonstrate that anaphylaxis after ingestion of berries can also occur in patients with sensitization to PR-10 proteins only.

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TRENDS IN CONTACT DERMATITIS

TP0896 | Metal allergy related to the use of orthopaedic prosthesis after trauma and normal aging process

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Background: Metal hypersensitivity is very common, especially to nickel sulphate, which is contained in many objects and substances we use on a daily basis. The steady increase of metal allergies related to the use of orthopaedic prosthesis after trauma and normal aging process, led us to carry out this study. We performed some tests before patients underwent hip, knee, shoulder replacement intervention. Those tests aim at evaluating if there might be a risk for metal allergy post intervention.

Method: We have developed a protocol based on the medical history and patch testing (Lofarma SpA - Milano), so as to evaluate metal hypersensitivity. Primary care checks have been carried out with x-ray and clinical evaluation, the latter via visual analogic scale (VAS).

Results: Out of 94 patients awaiting prosthesis, a high level of allergy has been found out, indeed: 15 patients were positive to nickel sulphate, cobalt sulphate and chromium sulphate, 6 patients were positive only to nickel sulphate and cobalt sulphate, 2 patients were positive only to titanium oxide (Patch Test Lofarma SpA - Milano). The follow up was carried out on four years. No patient reported any reaction related to hypersensitivity or complications after implant.

Conclusion: With a preventive activity performed via patch tests, it is therefore possible to diagnose not only a specific allergy, but to lead surgeons towards the best choice of prosthesis for the needs of patients. Prostheses are composed of sliding surfaces that inevitably produce friction: depending on the materials they are made of, cobalt, nickel, chromium, titanium, these can release particles that may trigger an inflammatory reaction (local or generalized) or an allergic reaction. In fact, allergies are among the main complications that arise after a prosthetic operation, sometimes making a second intervention necessary. A timely and careful diagnosis in cases of doubtful sensitivity, can avoid this type of problems, which cause discomfort to the patient.

The choice of modern hypoallergenic implants can help prevent any kind of potential reactions.

TP0898 | Is atopy a predisposing factor for contact hypersensitivity – results from patch testing unit of 200 consecutive patients

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Background: It is known that atopic individuals have higher levels of IgE in their blood; therefore, they have predisposition to certain allergic reactions. All our patients were referred to patch testing, every one of them had some kind of underlying skin condition. Contact hypersensitivity is a type IV allergic reaction (cell-mediated) and Patch test (PT) is the gold standard in proving this type of allergic reaction in patients. By comparing the results from Patch test of atopic and non- atopic referred patients, we want to test if atopic patients have higher frequency of contact sensitivity.

Method: We conducted a study with 200 patients (atopic and non-atopic), all of whom were referred to patch testing to our clinic for a period of time from 2011 until 2015. They were tested with a series of 30 allergens -European Baseline. The results were evaluated on the 2nd and the 3rd day. Irritative reactions were considered negative. For the statistical analysis SPSS v22, level of significance 0.05, confidence interval 95% were used.

Results: Out of all 200 tested patients, 122 (61%) have a positive reaction to one or more than one allergens. The people with personal atopy are 77. Among them 46 (61%) had a positive PT reaction. The most common body parts which were involved were hand (49.4%) and eyelid (24.7%), and the most common allergens were Nickel (57%) and Fragrance mix I (21.3%). According to the statistics there was observed no significant difference between the number of allergens (positive PT) and the presence of an underlying atopy. We have no evidence of impact on the strength of the reaction by the presence of atopy (*P*-values for 2nd and 3rd day close to one). By using Chi-squared test, we wanted to find if atopic individuals who were exposed to allergens have more positive PT results, compared to no- atopic patients. However, statistics show that there is no significant relationship between exposure and positive PT results in atopic patients. Statistic results show no relationship between hypersensitivity to more than one allergen and the presence of atopy (*P*-value 0.444).

Conclusion: In our study atopic patients do not show higher sensitivity to PT compared to no-atopic patients. The presence of personal atopy gives no reason for patients to be referred to patch testing.

TP0899 | The morph of an irritant contact dermatitis into an allergic dermatitis

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Case report:

Background: While irritant contact dermatitis results from exposure to substances that produce irritation of the skin, allergic contact dermatitis is a delayed hypersensitivity reaction following topical exposure to an allergen. Sometimes this demarcation is barely theoretical and the transformation of one into another is a challenge for the dermatologist, for both diagnostic approach and therapeutic conduct.

Method: We report the case of a 47-year-old female patient presenting in the dermatology clinic for the presence of large, well-demarcated erythematous scaly plaques located on the knees and extended to the calves despite of the corticosteroid (topical and systemic) and antihistamine therapy. The patient also presented erythematous papular distant lesions in the facial, thoracic and axillary area. The lesions appeared after wearing a polyester-styled clothing that was in direct contact with the lower limbs. The patient did not stop using this synthetic material for 2 weeks, which is why we raised the suspicion of irritant contact dermatitis which turned into allergic contact eczema. The lesions extended in spite of systemic corticotherapy and this could can be explained by maintaining the possible triggering factor in different clothing articles that have polyester in composition. With the removal of the alleged trigger factor, the patient's progress was favourable.

Results: In this case, the clinical picture was extremely suggestive of an irritant contact dermatitis but the difficult anamnesis and the unfavourable evolution under corticosteroids raised etiological problems. With the suspicion of a possible triggering factor such as polyester fibres contained in the trousers that the patient continues to wear, simple measures in order to remove this trigger factor led to a favourable therapeutic response.

Conclusion: Regarding the form of contact dermatitis, we consider that initially the patient was confronting an irritant dermatitis, which, following the alteration of the skin barrier, turned into an allergic form, certified by the presence of distant lesions. After complete remission of the lesions and stop of corticoid and antihistamine therapy the patient will be allergological re-evaluated for complete skin patch tests.

TP0902 | Airborne contact dermatitis and hand eczema caused by 2-Hydroxyethylmethacrylate (2-Hema)-case report of occupational contact allergy

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Case report:

Background: The first case of contact dermatitis caused by methylmethacrylate has been reported in 1941. Acrylates were commonly considered to be occupational contact allergens, particularly in dentists and orthopaedic surgeons, since dental materials and bone cement contain (meth)acrylates (1). However, in the recent year, the demand for long-lasting cosmetic nails has led to the widespread use of gel nail polishes and acrylic nails, that contains acrylates.

Clinical case: A 37 years old woman, who has been working as manicurist since 15 years, was forwarded to our clinic with hand eczema and facial dermatitis for 5 months. In the past one month the symptoms have increased in intensity. There were no signs for rhino-conjunctivitis or asthma. The performed patch testing showed positive reactions to 2-hydroxyethylmethacrylate (2-HEMA) and ethyl acrylate. The patient refused to change her occupation. Her condition improved significantly once she started to use regularly personal protective equipment.

Conclusion: Acrylates are not included in European baseline series for patch testing. The prevalence of allergy to acrylates is increasing, especially amongst the population involved in the beauty industry. It also affects consumers of gel nails/acrylic nails.

Reference: (1) Romaguera C, Grimalt F, Vilaplana J. Methylmethacrylate prostheses dermatitis. Contact Dermatitis 1985: 12:172-183.

TP0903 | Short exposures and glove protection from (meth)acrylates in nail beauticians – thoughts on a rising concern

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Background: Allergic contact dermatitis (ACD) from (meth)acrylates in nail aesthetics is a rising concern, namely in the occupational setting.

Method: We performed patch tests (PT) with the interposition of glove fragments between the PT test chamber and patients' skin for different time periods, in 3 patients with occupational ACD and positive PT to the (meth)acrylates and negative PT to gloves.

Results: In case 1, the patients' long-lasting nail gel polish (Shield™) gave a positive reaction (1 + or 2 +) after 4 hours exposure in the areas protected with all types of gloves. When exposure was prolonged for 24 h, there was a 2 + to 3 + reaction extending to the whole 3 × 3 cm area of contact with the glove fragment where the patch test chamber had been applied.

In case 2, exposure to the patients' nail gel and to HEMA through nitrile and latex gloves for 30 min and 60 min was negative at the D3 and D7 reading, but PT with HEMA applied directly on the skin only for 30 min was positive (1 +).

In case 3 there was a strong positive reaction to HEMA (2 +) when the PT chamber was applied directly to the skin for 30 minutes, negative when tested over nitrile gloves for 30 minutes, but positive (1 +) when exposure time over gloves was extended to 60 minutes.

Conclusion: Gloves do not completely prevent elicitation of an allergic response to (met)acrylates and there is some interindividual variability: nitrile gloves prevented the reaction to HEMA after 1 hour exposure in a patient with the less intense reaction (1 +) but not in the patient with a 2 + reaction. Nevertheless, this patient was still protected during 30 min. So we could suggest the use of nitrile gloves for a maximum of 30 minutes and then replace them if the procedure was not finished. A 30 min exposure to HEMA was enough to elicit a positive PT in 2 individuals. There are no studies about the application time needed for (meth)acrylates to penetrate the skin but a 30-min exposure may be enough. Were this fast penetration proven for all the other allergens, a shorter allergen application might facilitate the PT technique, particularly in hot countries or in patients exposed to high temperatures at work, where a 2-day occlusion may be cumbersome. In conclusion, short contacts with HEMA (<30 minutes) allows enough skin penetration into the epidermis to elicit a positive PT, suggesting that very short exposures or minor amounts going through gloves can elicit ACD in the occupational setting.

TP0904 | Occupational contact dermatitis in three adolescent males in the differential diagnosis of raynaud phenomenon

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Case report:

Background: Raynaud's phenomenon (RP) is characterized by episodic and reversible vasospasm of the extremities provoked by exposure to cold or emotional stress. In cold exposure, the color of the fingers changes to blue and white followed by red color change during rewarming. Occupational contact dermatitis (OCD) is the major work-related cutaneous disorder generally located in hands which are the most common body parts exposed to chemicals.

Case series: Three adolescent males admitted to our hospital in the winter months with complaints of swelling and color change in their both hands. They were directed to the pediatric rheumatology clinic with the suspect of RP. Patient 1 was complaining from a 3-week swelling which was increasing towards the end of the workday and his hands were becoming itchy when rewarmed. His hands were erythematous and there was a burn scar on his right hand along with small ulcerations. He had been working as a welder for the last 3 months where his hands were being exposed to methane gas. The complaint of Patient 2 was swelling and erythema in his hands for the last 2 weeks. His hands were becoming painful and itchy when he got warm. In physical examination, the 3-5th fingers of his left hand seemed more erythematous and swollen. The findings were consistent with the red phase of RP which occurs during rewarming. However, he mentioned that cold was not a trigger. He was an auto mechanic not always wearing his gloves and his left glove was torn exposing 3-5th fingers of his left hand directly to the chemicals. Patient 3 complained from a 2-week swelling in his hands. He was a battery industrial worker. In physical examination, his hands were swollen and purple; however, both thumbs were spared. Because of the current occupational history, exacerbation of the complaints towards the end of the workday, and absence of provocation with cold, we suspected OCD in these patients.

Conclusion: These patients were directed to the pediatric rheumatology clinic with the primary diagnosis of RP. However, the complaints were atypical for RP and careful history investigation revealed their current occupational exposure to chemicals which led us to the correct diagnosis as OCD. When the onset of the symptoms is in the winter, contact dermatitis localized to hands could be misdiagnosed as RP. The best approach is a thorough clinical assessment by means of meticulous history taking and physical examination to make a correct diagnosis.

TP0905 | Protein contact dermatitis in combination with chronic spontaneous urticaria and atopic dermatitis: A case report

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Case report: Introduction: Protein contact dermatitis (PCD) is a rare condition. It is an eczematous reaction occurring to large proteins in foods which penetrate compromised skin to cause an immediate reaction. PCD most frequently manifests as a chronic, recurrent, eczematous hand dermatitis. Main symptoms include itching and/or stinging within 30 minutes upon contact with the allergen. PCD

is considered to be a combination of immediate Type I and delayed Type IV allergic responses.

Case presentation: We present a 41-year-old female who was referred to our Clinic for diagnostic evaluation. She presented with a history of hand itching, stinging, redness and rash appearing shortly after a contact with tomatoes, eggplant, and zucchini. The patient reported the following additional symptoms: recurrent hives and angioedema, dry skin and pruritic rash on hands after sun exposure. Our diagnostic approach included SPT with foods (neg.) and prick to prick test with zucchini (neg.), and eggplant (positive). We performed a challenged test which was considered positive since the contact with eggplant caused erythema, edema, and pruritus. All laboratory results were within normal ranges. The patient was diagnosed with protein contact dermatitis to eggplant, chronic spontaneous urticaria and atopic dermatitis and was successfully treated with oral antihistamines, topical steroids, allergen avoidance, and emollients.

Conclusions: The precise incidence of protein contact dermatitis is unknown but probably is underrecognized and underreported. A better understanding of contact allergy to food may help identify some of the more elusive allergens responsible for difficult cases of contact dermatitis.

TP0906 | Contact urticaria in a baker after a long term wheat flour exposure - a case report

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Case report:

Background: Contact urticaria (CU) is an immediate wheal-and-flare reaction that appears on the skin usually within 30 minutes after external exposure to an allergen or irritant and disappears when the eliciting agent is removed. Food handlers are with increased risk for developing CU. When present, it could interfere with their everyday occupation. Our aim is to present a clinical case of CU to wheat flour in a female baker.

Case presentation: We report a case of a 49-year old female baker who was admitted to our clinic with a personal history of wheals and severe itch on her hands and forearms whenever she was working with wheat flour. Symptoms were usually appearing within an hour after contact with the flour. She has been working as a baker for 12 years but it wasn't until 12th year that the symptoms started. No extracutaneous involvement or signs of anaphylaxis were being observed. The patient has no personal or family history of atopy. Prick to prick test with wheat flour was performed and it was positive. A skin prick test to aeroallergens was also done and it showed no significant sensitization.

Conclusion: We find the following case interesting because of the relatively few reports of CU's occupational relevance in bakers and because of the long period of wheat flour exposure before the symptoms' start.

All data presented is with the patient's permission.

TP0908 | Non-invasive diagnosis of contact dermatitis by in vivo imaging

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Background: Two main forms of contact dermatitis (CD) are described: allergic (ACD) and irritant contact dermatitis (ICD), depending on the underlying immunological mechanism. ACD and ICD share clinical features and differential diagnosis is limited by the lack of a reliable and reproducible diagnostic method. The purpose of this study is to evaluate the main histological, molecular and cellular characteristics that could discriminate ACD and ICD in order to identify diagnostic biomarkers. Our final goal is to develop a non-invasive approach by *in vivo* confocal microscopy to reliably differentiate both types of CD.

Method: We capitalized on murine models of ACD and ICD induced by the topical application of referenced allergens and irritants. We then performed histological, molecular, cellular and confocal microscopy analyses using histology, qPCR, flow cytometry, immunohistochemistry and a *in vivo* confocal scanning microscope device.

Results: Our results confirmed that histology is not a reliable method to discriminate ACD and ICD. In contrast, ACD and ICD have clearly distinct molecular signatures: signatures of adaptive immunity T characterize the allergic response. We next demonstrated that a significant number of CD8 T cells infiltrate the epidermis in ACD lesions but not in ICD and are necessary to initiate the allergic response. We then sought to identify epidermal immune cells by confocal microscopy. Their identification using the fluorescent mode allowed us to determine their position in the tissue. We are currently performing analyses to detect them using reflectance mode only.

Conclusion: Epidermal infiltration by CD8 + T lymphocytes is the main parameter to discriminate ACD from ICD. Nevertheless, further investigations are necessary to sensitively distinguish their presence or activity using reflectance microscopy.

TP0909 | Isobornyl acrylate- contact allergen in continuous glucose sensor system

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Background: Continuous glucose sensor systems mark a significant change in life quality of patients with diabetes. Repeated self-monitoring of blood glucose-levels by finger pricking can be omitted. Interstitial glucose levels are measured by an intradermal catheter, which is sticked with an adhesive patch to the skin. Contact dermatitis is reported increasingly to the device.

Method: Epicutaneous testing was performed in 4 patients with suspected contact dermatitis: Standard, acrylates, adhesive contact allergens and Isobornyl acylate (IBOA) 0.1% in petrolatum.

Results: In 3/4 cases isobornyl acrylate was strongly positive. One patient had no contact allergy and healed after moisturizing the skin.

Conclusion: IBOA is the culprit contact allergen of the sensor device. 23 patients complaining of contact dermatitis using the same flash glucose monitoring system were published since 2017. In some of these ethyl acrylate, ethyl methacrylate, hydroxy ethyl methacrylate, hydroxypropyl acrylate and epoxy resin, abitol, hydroquinone showed positive test reactions. In our patients IBOA was the only contact allergen to be detected and showed no cross-reactivity to other acrylates.

TP0910 | Anti-inflammatory activity of humic acids in murine model of allergic contact dermatitis

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Background: Allergic contact dermatitis (ACD) is a highly prevalent inflammatory disease of the skin caused by an allergic reaction to a substance with symptoms such as pruritus, red, swollen. As a result of the complex etiology in ACD, therapeutic compounds lack efficacy and lead to numerous side effects. In this respect, peloid-derived humic acid (HA) deserve particular attention. The aim of our study was to evaluate the anti-inflammatory activity of a topically applied HA in the treatment of ACD in murine model.

Method: Aqueous HA cream (5%) produced by blending appropriate quantities of HA and additional water into emulsifying ointment BP. For induction of ACD-like skin disorders, 2.4-dinitrochlorobenzene (DNCB) was applied onto the BALB/c mouse dorsal skin. Induction of ACD was achieved by topical application of 100 μL 1% DNCB in 4:1 acetone/olive oil solution once daily to the shaved dorsal skin. These procedures were repeated for 3 days and followed by a period of no treatment for 5 days. In the second challenge, mice sensitized with DNCB were treated with HA cream 3 h prior to the application of 0.5% DNCB (days 8-16). Mice in the control group for ACD received vehicle treatment alone without DNCB treatment. Following challenge for 7 days, the mice were sacrificed on day 17 of the experiment. Skin tissues from the backs of the mice were excised and subjected to histological examination, and blood was collected in heparinized tubes from cardiac puncture. Total serum IgE levels of ACD mice were measured by ELISA.

Results: Topical application of HA reduced ACD based on histological analysis and serum IgE levels. HA inhibited mast cell infiltration into the skin tissues and serum histamine level. HA suppressed DNCB-induced expression of INF-γ, IL-4, IL-5, IL-10, IL-13, IL-17 and TNF-α in the ACD tissue. Overall, HA significantly inhibits pathways that lead to inflammatory cell infiltration and the production of inflammatory cytokines in the skin. Thus, HA treatment results in anti-inflammatory effects capable of inhibiting ACD by inducing immunosuppressive responses.

Conclusion: HA exhibits anti-inflammatory effects in ACD mice by regulating inflammatory mediators. These results demonstrate that the HA is a promising therapeutic for ACD and provides new insights into the role of humic substances and natural organic matter in the control of cutaneous immune responses potentially relevant to a broad range of allergic and inflammatory skin diseases.

SUNDAY, 2 JUNE 2019
TPS 17
EPIDEMIOLOGY OF FOOD ALLERGY I

TP0911 | Substantial variation in food allergy prevalence and causative foods in adults across Europe

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Background: Prevalence of self-reported food allergy ranges from 1% to 19% for foods frequently consumed and commonly implicated across Europe. Data on prevalence of clinically manifest food allergy are lacking, especially in adults, and incomparable study protocols hamper accurate evaluation of intracontinental differences. The aim of this study was to determine the prevalence of food allergy, defined as symptoms plus sIgE-sensitisation, to 24 relevant foods in adults across Europe, using a standardised protocol.

Method: In the EuroPrevall project, a pan European study investigating the prevalence of food allergy, a screening questionnaire was sent to a random sample of the general adult population in eight European centres. All responders reporting symptoms to one of 24 pre-selected commonly implicated foods and a control group consisting of a random sample of responders who did not report symptoms to any of the selected foods, were invited for broader evaluation, comprising an extensive questionnaire on reactions to the 24 selected foods, and measurement of sIgE against these foods. Multiple imputation was performed to estimate missing symptom and serology information for non-responders.

Results: Overall prevalence of food allergy was highest in Zurich at 5.6%, followed by 3.3% in Madrid, 2.8% in Lodz, 2.1% in Utrecht, 1.4% in Reykjavik and 0.3% in Athens. In Zurich, Lodz and Utrecht, the highest prevalence was found for hazelnut (respectively 2.6%, 1.3% and 0.9%), peach (respectively 2.0%, 0.5% and 0.6%) and apple (respectively 1.9%, 0.8% and 0.9%). Peach was also one of the top three causative foods in Madrid (1.6%), along with melon (1.0%) and shrimp (0.8%); and in Athens (0.1%), along with walnut (0.3%) and sunflower seed (0.1%). In Reykjavik, the highest prevalence estimates were found for banana (0.5%), carrot (0.4%) and shrimp (0.4%).

Conclusion: Food allergy shows substantial geographical variation in prevalence and causative foods in adults across Europe. Although food allergy defined as symptoms plus sIgE-sensitisation was less common than self-reported FA, prevalence still reached 6% in parts of Europe. Plant foods dominated as most common causative foods, with the exception of shrimp in Spain and Iceland, suggesting that prevalence is likely related to pollen exposure and possibly consumption.

TP0912 | Characteristics of food allergy in children: National multicenter study

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Background: Food allergies impose a significant burden on the life of the child and the family. In this study, to determine the demographic characteristics of food allergies, we investigated the characteristics of patients with food allergies in different regions of Pediatric Allergy-Immunology departments in Turkey.

Method: Turkey's National Study of Allergy and Clinical Immunology Society has conducted a Study Group on Food Allergies. 25 centers participated in this multicenter, cross-sectional and descriptive study.

Results: A total of 1248 children were included in the study (62.0% boy, 38.0% girl) consisting IgE-mediated, non-IgE mediated and mixed-type cases of food allergy in a percentage of 71.8%, 16.1% and 12.1%, respectively.

In the IgE-mediated group, the age of onset and diagnosis were 8.26 ± 16.98 months and 13.73 ± 24.58 months, respectively, and 64.7% of the cases were male. The most common types of food allergy were egg white, cow's milk, egg yolk and hazelnut. The most common initial symptoms were urticaria-angioedema, eczema and anaphylaxis. There was no relationship with the family history of atopy.

In the non-IgE mediated group, the age of onset and diagnosis were 4.51 ± 11.21 months and 7.16 ± 12.82 months, respectively, and 54.2% of the cases were male. Milk, eggs, beef and wheat were generally responsible for this type of atopy mostly admitting with proctocolitis.

In boys and in children whose parents have low level of education, the commonest type of food allergy was IgE-mediated ($P < 0.01$ for each). Non-IgE-mediated food allergy found to be significantly more frequent in girls and in the families with good income ($P < 0.01$ for each).

Conclusion: In this study, clinical characteristics and risk factors and phenotypes of food allergies in Turkey were investigated.

TP0913 | Clinical features of 4458 food allergic children from 5 year's registry

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Background: The purpose of this study is to clarify clinical features of food allergy (FA) among Japanese children by using database registry at our department.

Method: We have previously established the database registry system on immediate type of food allergy (FA) patients from 2008. The system can integrates the sequential information on medical history, Ag-IgE, SPT and oral food challenge (OFC). We have analyzed the 5 year's database from 2010 to 2014. The database included total of 4458 patients. The median age of FA diagnosis was 7 months old and that of 1st immediate allergic reaction 10 months old. The numbers of patients with the history of immediate type of allergic reactions and anaphylaxis (An) by their past history or OFC were 3.906 (88%) and 1.756 (39%), respectively.

Results: There were 10 703 registered food allergens. The number of allergens with immediate type reactions was 6356 (59%). OFC was performed 7205 times and 2535 of them were positive. Concerning itemized food allergens, Hen's egg (HE), cow's milk (CM), peanut (PN) and wheat (W) were major allergens and that ratios of HE/CM/PN/W per registered whole allergens were 27%, 17%, 10% and 10%, respectively. The ratio of An per immediate histories, CM, PN, W and buckwheat (BW) were significantly higher and the ratios of CM/PN/W/BW were 51%, 49%, 46% and 44%, respectively ($P < 0.05$). The ratio of past history of using adrenaline injection per immediate histories about CM, PN, W and BW were 16%, 15%, 12% and 12%, respectively ($P < 0.05$). There were 2978 food allergens which had acquired tolerance during the 5 years. Ways to acquire tolerance were by dietary instruction without OFC (33%), dietary instruction based on OFC results (60%), and judgement of sustained unresponsiveness after oral immunotherapy (7%), respectively.

Conclusion: By using the large database, we could obtain the real clinical features of immediate type FA (mostly challenge proven), incidence of An and rates of tolerance acquisition during the 5 years. Furthermore, prevalent severe allergic reactions can be recognized in CM, PN, W and BW in Japan.

TP0914 | Profilin sensitization – a review of 5 years follow up in an allergy department

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Background: Profilin is a minor allergen ubiquitously spread in pollen and plant food species. It can show cross reactivity between

distantly related species, being responsible for many allergic sensitizations. The prevalence of profilin sensitization in pollen allergic patients in European countries has been estimated to be 10-30%. Although this pollen-food syndrome is frequently mild (oral allergic syndrome: OAS) more severe reactions might occur.

Objective: To evaluate clinical evolution over a 5 years (y) period of a group of patients sensitized to profilin.

Method: In a 4 months period, patients with positive skin prick tests (SPT) to pollens, fruits or vegetables, performed SPT to profilin and LTP. The ones who were sensitized to profilin were selected, excluding co-sensitization to LTP to avoid bias. Evolution of symptoms, SPT, sIgE and ImmunoCap® ISAC were reviewed in a 5-year period.

Results: From a sample of 233 allergic patients sensitized to pollens/fruits/vegetables, there were 19 patients (8%) sensitized to profilin and 14 of them didn't have LTP co-sensitization (median age 25 years, 77% male). One was excluded due to lack of data. The median follow up was 5 years (range: 2-5 years). All 13 patients had rhinitis and were sensitized at least to grass pollen; none were under specific immunotherapy. Five of 13 patients (38%) had food allergy (FA) at the beginning: OAS (3), mucocutaneous manifestations (1) and isolated gastrointestinal symptoms (1). There were 3 cases of FA to melon, watermelon and peach; 2 to apricot, cherry, apple, pear, banana and orange and 1 to fig, kiwi, pineapple, lettuce and cress. Three patients had molecular allergen profile (primary sensitization to pollens, mainly grass, and cross reactivity between profilin); 4 patients maintained FA, one acquired tolerance and one has developed OAS after 3 years of follow up. There weren't new FA to fruits or vegetables in the remaining 214 patients.

Conclusion: The profilin sensitization prevalence is lower than expected and rises the need to perform large prevalence studies in the portuguese population. As expected, only less than 40% had FA and all reactions were mild. It was not found any parameter, including the molecular pattern of sensitization, with prognostic value regarding tolerance or FA acquisitions.

TP0915 | LTP's sensitization – a 5 year follow up study

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Background: Nonspecific lipid transfer proteins (LTP) are among the most important panallergens in pollen/plant food allergic patients. However, sensitization profiles and clinical manifestations vary widely between allergic patients. Our aims were to assess the frequency of sensitization to LTP (Pru p3) and investigate the onset of new food allergies (FA) in these patients.

Method: For 4 months, all patients with positive skin prick tests (SPT) to pollens/fruits/vegetables were tested to LTP and profilin. LTP sensitized patients were clinically evaluated over a 5 years period. Patients co-sensitized to profilin were excluded.

Results: 233 patients were included, 32 (14%) mono-sensitized to LTP, 5 co-sensitized to profilin and 196 with negative SPT to LTP. In the study group (56% males, median age 25 years), 30 (94%) had at least one atopic disease and 27 (84%) had positive SPT to pollens. At the initial evaluation, 24 of these 32 patients had FA, 20 (83%) to *Rosaceae/Prunoideae*, 9 (38%) to tree nuts and 6 (25%) to peanut. Twelve patients experienced symptoms following ingestion of more than one LTP-containing plant-derived food. Half of the sample had anaphylaxis. In the follow up period 14/24 (58%) developed new FA, 8 (57%) had anaphylaxis at the initial evaluation comparing with 4/10 (40%) who did not experience new FA reaction ($P = 0.41$). Four reported systemic symptoms with previously tolerated foods. Most new allergies were caused by *Rosaceae/Prunoideae* (n = 17), other fruits/vegetables (n = 15) and tree nuts (n = 3). Of the 32 patients sensitized to LTP, 8 didn't have FA, 88% had positive SPT to pollens and all remain asymptomatic. Baseline *Pru p3* IgE levels did not differ significantly between patients with oral allergy syndrome or systemic symptoms ($P = 0.99$), neither between patients who developed new FA or who did not experience new FA ($P = 0.42$).

Conclusion: In agreement to literature, *Rosaceae/Prunoideae* were the most commonly implicated in LTP syndrome. During the 5 years follow up, more than half of the FA patients developed new allergies against previously tolerated foods. None of the evaluated parameters allow us to predict which patients will develop new FA. All the patients sensitized to LTP without FA remain asymptomatic and also there's no evaluated parameters that distinguish them from the other patients.

TP0916 | LTP and profilin co-sensitization: A 5 years follow-up

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Background: Profilins and Lipid transfer proteins (LTPs) are the panallergens with more importance in the pollen and plant food allergic patient's management. Our aims were to evaluate the frequency of co-sensitization to LTP and profilin in a group of patients sensitized to pollens/fruits or vegetables and investigate the onset of food allergies (FA).

Method: In 2013, for 4 months, skin prick tests (SPT) with LTP (Pru p 3) and profilin (Pho d 2) were performed to all the patients that had positive SPT for pollens/fruits or vegetables. The patients also filled a questionnaire to evaluate the presence of food allergy (FA) at

the moment. Patients co-sensitized to LTP and Profilin were selected and their clinical evolution was evaluated for over 5-years.

Results: 233 patients were evaluated, 5 (2.2%) were co-sensitized and four of them had no FA at baseline evaluation and maintained asymptomatic along the study. Only one patient had already FA and developed new ones on follow-up: a 32 years-old female with melon Oral Allergy Syndrome (OAS) and rhinoconjunctivitis. In the initial evaluation, SPT were positive for pollens, cat, LTP, profilin and melon. Months later she referred cutaneous pruritus when peeling peach and OAS for tomato and cherry. SPT for peach, strawberry, plum, cherry, apricot, apple, tomato and nectarine were positive. At the time, she ate apple without symptoms. Two months later, the patient referred OAS with apple skin and an anaphylactic reaction with pomegranate. Pomegranate's prick-prick tested positive. The molecular profile ISAC was positive for cross-reactivity components LTPs and Profilin. Months later she referred a new cantaloupe OAS. She initiated Pru p 3 SLIT and had recurrent lip angioedema during the build-up phase, only achieving the target dose on the 5th month. She referred new OAS with lettuce 4 days after starting the SLIT and with watermelon 10 months after. The patient is currently under SLIT for 14 months without intercurrences and has already eaten cherry again without symptoms.

Conclusion: In our sample co-sensitization doesn't seemed to be a determinant factor for the development of FA given the fact that four out of five patients co-sensitized to LTP/Profilin stayed asymptomatic and only one developed FA. Pru p 3 SLIT seems to be already inducing tolerance to some previously sensitized foods. In order to find the culprit to each new symptom future inhibition studies should be performed.

TP0917 | Sensitization profile and severity of reactions of patients with LTP syndrome from two mediterranean areas with different pollen profile

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Background: Patients with allergy to nsLTP form a heterogeneous group in terms on sensitization profile and severity of the symptoms. This heterogeneity could be due to the geographical distribution and the presence of additional allergies to pollens, such as profilins that has been associated with a decrease in severity. The aim of this study was to analyze the sensitization profiles and severity of reactions of patients with LTP syndrome from two Mediterranean areas with different pollen exposition.

Method: Patients with diagnosis of LTP allergy from the Allergy Unit of the Regional University Hospital of Malaga (RUHM) and Clinic Hospital, Barcelona (CHB), Spain during 2014-2017, were prospectively included. All patients reported at least one episode after the intake of peach, positive skin prick test (SPT), specific IgE and/or a double blind placebo controlled food challenge (DBPCFC) with the culprit food. Patients were classified in two groups: (a) Monoallergic: Those that presented a reaction just with peach: (b) Polyallergic: Those that presented reaction with at least 2 plants-food related with LTP (PFrLTP).

Results: From 293 patient finally included, 206 (70.3%) were female with a median age of 38.92 years. From these 18 (6.1%) were classified as monoallergic and 275 (93.8%) as polyallergic. From monoallergic group, 11 (61.1%) had oral allergy syndrome (OAS) or Urticaria-Angioedema and 7 (38.9%) anaphylaxis. From polyallergic, 56 had anaphylaxis after peach intake, 228 had OAS or Urticaria-Angioedema. Comparing patients from HRUM versus CHB, olive (61.1 vs 27%; $P = 0.01$) and profilin (26.9 vs 8.2; $P = 0.001$) sensitization were significantly higher in Malaga population. Moreover, in patients with profilin sensitization we found fewer anaphylaxis (10.7% *vs* 22.7%; $P = 0.05$). According to the number of PFrLTP implicated, monoallergic group had a higher percentage of anaphylaxis compared to polyallergic group (41.2 *vs* 18.3; $P = 0.001$).

Conclusion: The most important difference between both populations from different geographical areas is the sensitization to profilin that seems to reduce the severity of the reactions whereas patients with a monosensitization profile show more severe reactions.

TP0918 | Oral food challenges to nuts in children with LTP sensitization

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Background: The aim is to evaluate the safety and efficacy of open oral food challenge (OFC) to nuts in children with lipid transfer protein (LTP) sensitization applying a modified allergen-reduced protocol.

Method: A retrospective four-year (2014-2018) observational study of children (2.5-16.5 years old) with a history of: a. IgE-mediated reaction to nuts, b. IgE sensitization to nuts at the evaluation of food allergy in children with atopic dermatitis (AD), c. IgE-mediated reaction to food other than nuts, and Pru p 3-specific IgE value ≥ 0.10. We studied: sex, age, personal history of atopy, maximum wheal diameter from skin prick tests, prick to prick, specific IgE to extract/allergen molecules in walnut, peanut, almond and hazelnut, cofactors and OFC's outcome. According to our protocol, a total of 1.48 gr (±0.10) of nut protein was administered in four incremental doses at 20 minute intervals.

Results: 53 children (75% males) mean age 4 years old (±2.64) at reaction time and mean age 8.1 years old (±3.45) at challenge time were included. 35 children (66%) reported an IgE-mediated reaction (20% cofactor presence), the rest were found only with sensitization. Mean total IgE's value was 1068 KU/L CI[757, 1379]. At 14/53 Cor a 9 > 0.54, <8.43, Cor a 14 > 0.75, <3.94 and 4/53 Jug r 1 > 0.39, <0.7 were determined. A total of 125 OFCs were done: 21 to walnut, 29 to peanut, 43 to almond and 32 to hazelnut (5 to praline). 5 (4%) were positive: 3 to hazelnut (2 to praline) with an episode of vomiting (history: 1 anaphylactic reaction to hazelnut, 1 mild reaction to another nut, 1 only sensitization), 1 to almond with anaphylactic reaction (history of anaphylaxis to another nut), 1 to peanut with an episode of vomiting (history of mild reaction to peanut). All children with a positive challenge had a history of AD. Children with Pru p 3 < 2.75, Cor a 9 < 8.43, Cor a 14 < 3.94 and Jug r 1 < 0.7 did not react. Also 79% of successfully challenged children had a history of AD.

Conclusion: OFCs to nuts in children with LTP sensitization with the modified protocol for the administration of incriminated food are safe and successful. History of AD and Pru p 3 > 2.75 were related to higher probability of reaction during OFC. Correlation of cosensitization to seed storage proteins (Cor a 9, Cor a 14, Jug r 1) and probability of reaction needs further investigation.

TP0919 | Co-sensitization patterns in children with tree nut and peanut allergy

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Background: To describe the patterns of co-sensitization to peanut and tree nuts(TN) in children with a history of IgE TN allergy.

Method: Retrospective study of children with reported reactions consistent with IgE mediated TN allergy attending our clinic between 2015-2018. Reported reactions, maximum wheal diameter of Skin Prick Tests(SPTs), sIgE and allergen components(CRDs) results were recorded.

Results: 49 children (mean age = 5.8 ± 3.8 years, 80%males) were included. 71 reactions were recorded; hazelnut was the most commonly implicated TN (n = 18, 37%). SPT to all TN were performed in 38 children with the following sensitization rates (≥3 mm): peanut:29(76%), walnut:27(71%), cashew and pistachio:26(68%), hazelnut:25(66%) and almond:19(50%). Thirteen (34%) children were positive to six TN, 4(11%) to five, 6(16%) to four, 6(16%) to 3, and 5(13%) to 2. The following patterns are described having the first TN as positive: Almond-hazelnut:100%, Cashew-pistachio (and viceversa):96%, Almond-peanut and Walnut-peanut:95%, Hazelnut-walnut:92%, Walnut-hazelnut:85%, Walnut-peanut:85%, Cashew/Pistachio-peanut:81%. 28 children had sIgE results for all TN. Sensitization rates were: hazelnut, peanut, cashew and pistachio 21(75%), walnut and almond 18(64%). 13 children (54%) were sensitized to all TN, 4(14%) to five, 3(11%) to four, 2(7%) to 3 and 2(7%) to two TN. The most common pattern was peanut- cashew-pistachio in 4(11%) children. The following sIgE patterns were observed when the first TN was positive(≥90%): Hazelnut-peanut (and viceversa) and Cashew-pistachio (and viceversa):95%, Walnut-hazelnut, Walnut-peanut, Almond-hazelnut, Almond-peanut, Almond-cashew/pistachio: 94%, Hazelnut-cashew/pistachio (and viceversa):90%. 28 children had CRD results but only two had the full panel tested. Co-sensitization patterns for CRD are shown in table 1.

Conclusion: Co-sensitization to TN is common in children with IgE reactions to TN and follow specific patterns. The clinical relevance of these patterns requires further investigation.

TABLE 1 Patterns of CRDs co-sensitization (rows) in children with positive CRDs (columns)

	Anao3	Arah1	Arah2	Arah3	Arah9	Jugr1	Jugr3	Cora9	Cora14	Cora8
co-Anao3		6/6	8/10	6/6	4/5	6/7	3/4	8/11	6/7	5/5
co-Arah1	6/8		6/10	6/6	4/6	6/9	4/6	6/9	5/6	5/5
co-Arah2	8/10	6/8		7/7	6/7	9/10	5/6	11/11	7/7	6/6
co-Arah3	6/10	6/8	7/12		5/8	5/10	4/7	7/11	5/7	6/6
co-Arah9	4/6	4/5	6/7	5/5		5/5	7/7	6/7	3/3	5/5
co-Jugr1	6/8	6/6	9/11	5/6	5/8		5/7	8/10	6/6	4/5
co-Jugr3	3/5	4/4	5/7	4/4	7/7	5/9		5/7	3/4	4/4
co-Cora9	8/8	6/6	11/11	7/7	6/7	8/8	5/6		12/12	6/6
co-Cora14	6/8	5/5	7/9	5/6	3/5	6/6	3/4	12/14		4/5
co-Cora8	5/5	5/5	6/8	6/6	5/7	4/5	4/6	6/9	4/5	

TP0920 | Surveillance of pollen-food allergy syndrome in elementary and junior high school children in northwest area of Saitama prefecture, Japan

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Background: The number of pollen-food allergy syndrome (PFAS) is increasing in children. The symptoms of PFAS may sometimes develop systemic allergic reactions, such as vomiting, diarrhea, wheezing and even anaphylaxis. However, there are few reports, and little is known on the prevalence, symptoms, and causative foods in children.

Method: We surveyed the prevalence of PFAS in a cohort of 2346 students (1157 boys, 1115 girls and unknown 74, 6 -15 yrs old, median 10.6 ± 2.58 yrs old) in elementary and junior high school in the northwest area of Saitama prefecture, Japan by employing a questionnaire. In this questionnaire, we defined PFAS as allergies to fruits and /or vegetables with an onset which occurred after the symptoms of allergic rhinitis (AR) appeared.

Results: The prevalence of PFAS was shown to be 6.9% (n = 161 among 2346 students). In children with PFAS, the mean ages in onset of AR and PFAS were 4.59 ± 2.76 and 7.38 ± 3.17 yrs old, respectively. The kind of causative foods for each subject was multiple (ranging 1 to 5 foods per person, mean 2.45 ± 2.51), and the number of affected students to each food were, from descending order, 68, 57, 41, 27,24, 23, 20, 12 and 11 for kiwi, pineapple, melon, peach, apple, watermelon, pear, tomato and banana, respectively (multiple answers were allowed). We observed the prevalence of allergic symptoms which were experienced among PFAS children by dividing them into local and systemic. As for local symptoms, the ratios of prevalence were 81.4%, 47.8%, 16.1%, 6.2% and 6.8% for oral, throat, ear, nasal and ocular symptoms, respectively (multiple answers were allowed). The ratios of systemic symptoms were 9.3%, 6.2%, 3.7% and 0% for respiratory, gastrointestinal, neurologic and cardiovascular symptoms, respectively (multiple answers were allowed). The ratios in the appearance of systemic symptom by each food were, from descending order, 48.1% (13 of 27), 33.3% (8 of 24), 33.3% (3 of 9), 33.3% (4 of 12), 31.6% (18 of 57), 30.4% (7 of 23), 29.4% (20 of 68), 29.3% (12 of 41) and 18.2% (2 of 11) for peach, apple, cherry, tomato, pineapple, watermelon, kiwi, melon and banana, respectively.

Conclusion: While it has been known that special kinds of foods such as apple and peach are likely to induce systemic symptoms, our results suggested that many kinds of fruits and /or vegetables could be the cause of systemic symptoms.

TP0921 | Determining health preferences of patients and families with food allergies

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Background: Oral immunotherapy (OIT) is a newly recommended therapeutic option for patients with food allergy, which has the potential to greatly improve quality of life (QoL). To justify the costs of this new treatment, it is important to translate the associated gain in quality of life into economic terms. QALYs (Quality Adjusted Life Years) are the gold standard to quantify the impact of a disease on quality of life. This project aims to develop a conversion algorithm (mapping) from a commonly used food allergy specific quality of life questionnaire (FAQLQ) to a generic QoL questionnaire (SF-6Dv2) to allow estimation of QALYs in patients referred for OIT treatment by their allergist.

Method: This cross-sectional study is based on QoL questionnaires filled in the context of application to a public academic OIT clinic in Montreal, Canada. In order not to influence their answers, applicants were explicitly made aware that the content of their answers would not be used in the prioritization process. FAQLQ questionnaires were administered as appropriate for age group. A standard SF-6Dv2 questionnaire was administered to teenagers and a modified version using a unitary approach was administered to all parents. SF-6Dv2 data were converted to QALY using preference weights developed by the University of Sheffield. The correlation between applicant characteristics and FAQLQ items with QALY was investigated using linear regression.

Results: As of December 2018, data from 739 patients had been entered in a database. The mean age was 7.2 (±4.3) years old. Five hundred fifty-two (75%) suffered from multiple food allergies and 279 (38%) were allergic to at least one ubiquitary food. The QALY value calculated from parents was 0.781 (95% CI: 0.773-0.789). The mean QALY value was 0.812 (95% CI: 0.787-0.837) according to teenagers and 0.801 (95% CI: 0.776-0.826) according to teenagers' parent. Significant correlations between applicant characteristics and QALY were the child's general health state and the presence of an ubiquitary allergy. QALY was most strongly associated with FAQLQ items describing physical suffering, emotional disturbance and holiday restrictions.

Conclusion: Measures of QALY value in food allergic patients referred for OIT were statistically different from the QALY value of the general teenager population. This project provides a quantitative basis for health economic analysis of new food allergy treatments.

TP0922 | Adolescents with a history of food allergy consume less milk, but not other calcium-rich foods, than their non-food allergic peers

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Background: Food allergy may impact diet quality and nutrient intake. Even previously food allergic children exhibit altered eating behaviours and food preferences, which can impact overall diet. Adolescence is a critical window for adequate calcium intake, due to intensive bone and muscle development, and the need to optimise peak bone mass. Little is known about dietary calcium intakes of adolescents with a history of food allergy. The aim of this study was to examine intake patterns of calcium-rich foods and supplements amongst adolescents with or without a history of food allergy.

Method: This study makes use of data from the Study of Allergy, Genes and the Environment (SAGE), a nested case-control study of the 1995 Manitoba, Canada birth cohort. In brief, 723 children were followed biennially from ages 7-8 to 12-14 years. At these visits, parents completed questionnaires on food allergy (including questions about food allergy in infancy and early life). At 12-14 years, adolescents completed detailed food frequency questionnaires, which included consideration of calcium rich foods (milk, ice cream, leafy greens), calcium fortified orange juice and multivitamin/mineral supplements. Intake patterns were defined as at least once weekly, vs less than once weekly. Logistic regression was used, with adjustments for maternal education, ethnicity and child's sex.

Results: In total, 472 adolescents (65% retention from baseline) were included in this study, of whom 60 (13%) had a history of food allergy. Compared to adolescents without food allergy, adolescents with a history of food allergy were significantly less likely to consume milk at least once a week (OR 0.39; 95%CI 0.19-0.79). In contrast, intake patterns of calcium-rich foods (e.g. ice cream/frozen yoghurt: OR 1.44; 95%CI 0.74-2.80; leafy greens: OR 0.85; 95%CI 0.34-2.14), calcium-fortified orange juice (OR 1.00 95%CI 0.53-1.87) and multivitamin/mineral supplements (OR 1.39; 95%CI 0.74-2.59) did not differ between the two groups of adolescents.

Conclusion: Manitoba adolescents with a history of food allergy ever consume less milk than their non-food allergic peers. Intakes patterns of other calcium-rich foods and supplements do not differ between the groups. However, these foods are higher in calories, or have a lower calcium bioavailability than milk. Dietary monitoring, with attention to both foods and nutrients is important for adolescents with food allergy.

TP0923 | Sensitisation and sero-reversion to tick bite induced galactose-1,3-alpha-galactose, meat and dairy sensitisation in New South Wales, Australia

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Background: Fox suppression programs have resulted in marked expansion of bandicoot and bush rat populations in New South Wales, Australia, greatly increasing human exposure to multiple tick bites on multiple occasions. Our laboratory has offered *in vitro* specific IgE testing for [Thermofisher Phadia ImmunoCAP] galactose-1,3-alpha-galactose (alpha-gal) for more than ten years. Clinicians' testing strategies have evolved considerably during this time. Our clinical experience has been that 40% of persons may return to eating meat after successful tick bite and meat avoidance over 24-36 months. We wanted to determine the incidence of alpha-gal tests, the frequency of positive tests and the rates of followup testing. We further wanted to assess the impact of a prior positive result on future test results in terms of increasing, similar or decreasing sensitisation.

Method: We interrogated our laboratory dataset for the ten years prior to January 2019 to determine the number of requests for specific IgE to alpha-gal, co-requested allergy requests as well as patterns of followup test requests. We then analysed the results of initial and subsequent tests for increasing or decreasing sensitisation over time. We only analysed data that included alphagal testing on each occasion, excluding persons who only had meat testing.

Results: 3485 unique persons had alphagal specific IgE testing of whom 1359 (39%) had values of > 0.35 kU/L, 313 (9%) had very low level sensitisation (between 0.10 and 0.35 kU/L with 52% less than 0.10 kU/L. 268 persons had multiple tests (1 had 8, 1 had 7, 2 had 6, 6 had 5, 15 had 4, 97 had 3 and 154 had 2) in our lab. Of the persons with multiple tests, 156 of 268 showed a marked decline in sensitisation, 55 remained similar and 57 had increased sensitisation. Most persons had concurrent specific IgE measurements for beef, pork, mutton and milk.

Conclusion: Only 19.7% of sero-positive patients had followup alphagal testing in our lab. Some may have had followup testing in other laboratories. The majority (58%) of persons with previous positive results who do have followup testing seem to be able to reduce their sensitisation. Many strongly sensitised persons show a relatively rapid decline (within 12-18 months) to levels where reintroduction of meat may be considered.

TP0924 | Is there a relation between legume protein consumption and the prevalence of legume sensitization?

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Background: Legumes vary considerably in their sensitizing potential and their allergic response. The reason behind this is not fully understood. Possible explanations could be consumption, exposure, and geographical background. Aim: To investigate if there is a correlation between legume protein consumption and the prevalence of legume sensitization. Additionally, the association between sensitization to specific peanut allergens and their concentration is investigated.

Method: Peanut, soybean, lupin, lentil, and pea sensitization data from scientific publications in the general population were analyzed in relation to consumption data obtained from multiple national food consumption survey databases. Data were stratified for children < 4 years, children 4-18 years, and adults (>18 years). Additionally, the national percentage of legume consumers was investigated. Furthermore, specific IgE sensitization data for peanut allergens were compared to the relative content of these allergens. Correlation was analyzed using WLS regression analysis and expressed as a r value.

Results: Analysis of all age groups together resulted in a low correlation between peanut sensitization and the relative consumption (r = 0.407), absolute consumption (r = 0.468) and percentage of consumers (r = 0.243). For soybean, no significant correlation was found between the prevalence of soybean sensitization and the relative consumption (r = 0.352), absolute consumption (r = 0.217) and the percentage of consumers (r = 0.007). The data of other legumes was not sufficient for statistical analysis. No correlation was found between relative concentrations of Ara h 1, 2, 3, 6, 7, and 8 and sensitization to these peanut allergens. Sensitization to Ara h 2 (70.7%) and Ara h 6 (71.2%) was high, while the concentration of these allergens is low (6.2% and 5.8%, respectively). In contrast, the concentration of Ara h 3 (70.6%) was high while sensitization was low (37.3%).

Conclusion: The results indicate that the amount of consumption plays a minor role, if any, in the prevalence of sensitization to legume proteins in all age groups. The concentration of specific peanut allergens in peanut did not correlate with the frequency of sensitization to these allergens. Other factors such as intrinsic properties of the proteins, processing, matrix, frequency, timing and route of exposure, and patient factors might play a more substantial role in the prevalence of peanut sensitization.

TP0925 | Lupine allergy in the chilean population: A cross-reactivity study with peanut allergy

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Background: Lupine is a legume with an interesting nutritional profile which has gained relevance due to its high protein content, emerging as an alternative to soy in the food industry. However, with the increased consumption of lupine, more cases of allergy have been reported, including episodes of anaphylaxis. Lupine allergy is IgE mediated and can be triggered by primary sensitization or as consequence of cross-reactivity with other legume' proteins. The latter has been more frequently observed in peanut-allergic patients. The prevalence of lupine allergy has not been reported in Chile yet, and it seems to vary in different populations. In this work we evaluated allergy to lupine in Chilean patients with peanut allergy and the cross-reactivity with peanut and other legume allergens.

Method: Twenty-three patients allergic to peanut were tested for lupine (*Lupinus spp.*), peanut (*Arachis hypogaea*) and soy (*Glycine max*) using skin prick test (SPT). The patient's sera were also tested for specific IgE levels to peanut, lupine, soy and pea. Some volunteers with positive skin prick test (SPT) and/or specific IgE levels to lupine also participated in a double-blind placebo-controlled open oral food challenge.

Results: Of peanut-allergic patients, 18/23 (78%) were sensitized to lupine, and of this group most of them presented co-sensitization with other legumes. 13 lupine-sensitized patients underwent double-blind placebo-controlled oral food challenge to lupine, to which 31% presented an allergic reaction. All the observed reactions were severe with some anaphylactic episodes.

Conclusion: Lupine sensitization and allergy in peanut allergy patients in Chile is high, including patients with severe lupine allergy at risk for anaphylaxis. Therefore, increasing education and awareness of potential lupine cosensitization and allergy risk in peanut allergy patients is warranted.

TP0926 | Study of the association between food allergic children and vitamin D levels

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Background: The incidence and prevalence of food allergies are increasing in Western world, yet underlying mechanisms are largely unknown. Food allergies reflect a lack of tolerance to food proteins. Genetic factors play a leading role in the development of food allergy and they interact closely with environmental factors. Studies have revealed a relationship between Vitamin D insufficiency and food allergy. It seems that low vitamin D status may influence the development of allergic disease. The aim of this study is to find the association between Vitamin D and total IgE levels in food allergic children.

Method: The study population consisted of 18 children. Food allergy diagnosis based on clinical criteria, questionnaires, skin prick tests and specific IgEs (ImmunoCap). Whole blood was extracted from the children involved. These results were then correlated with epidemiological data from each child such as weight, age and exposure to solar radiation. For this purpose, the Spearman rs correlation coefficient was used. In addition, the total IgE values were compared among children with adequate, insufficient and vitamin D deficiency with the Kruskal-Wallis statistical test. Further statistical analysis was performed with the help of the SPSS v20 program. Values $P < 0.05$ are considered statistically significant.

Results: Based on statistical analysis, a significant negative correlation between vitamin D and total IgE values was observed in children with food allergy (rs = -0.748, $P = 0.003$). Children with vitamin D deficiency showed statistically significantly higher total IgE levels compared to both children with vitamin D insufficiency ($P = 0.033$) and sufficiency ($P = 0.044$).

Conclusion: Children with IgE-mediated food allergy exhibit elevated total IgE while they have vitamin D deficiency. These data contribute to a better understanding of the development of food allergy and need further study. Our aim is to study more factors that are involved in the complex pathway of food allergy.

TP0927 | Prevalence of cofactor enhanced food allergy in the mediterranean area

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Background: The cofactors are independent factors of the allergen that favor the appearance of a severe allergic reaction. The most important are: exercise, alcohol consumption, nonsteroidal anti-inflammatory drug (NSAID) intake, psychological stress and others, such as menstruation.

Method: A descriptive, retrospective study of 11.975 patients from 2010 to 2017 was made. The selection criteria was positivity in the LTP skin test. We collected data on age, gender, related food intake symptoms (oral allergy syndrome (OAS), urticaria, angioedema, abdominal pain, anaphylaxis, anaphylactic shock) and age of onset, concomitant respiratory symptoms, presence of a cofactor (exercise, alcohol, NSAID), food groups involved and value of purified rPru p 3 allergen in patients with o without anaphylaxis/anaphylactic shock and asymptomatic patients.

Results: 379 patients fulfilled the selection criteria, 280 were adults and 98 children, 181 were males and 197 were women. The most frequently symptomatology presented was OAS and anaphylaxis. The average age of onset of food allergy symptoms was 26.10 years in adults and 5.97 years in children. Rhinitis and rhinoconjunctivitis were the most frequent concomitant respiratory symptoms. There was presence of a cofactor in 41 cases (28/41 involved the exercise). Nuts and fruits were the foods most involved in the reactions. In patients with anaphylaxis/anaphylactic shock the mean value of rPru p 3 vas 10.14 kU/l (6.41 kU/l in the others symptoms and 4.89 kU/l in asymptomatic patients).

Conclusion: 10.8% of patients sensitized to LTP presented a cofactor enhanced food allergy. The mean value of rPru p 3 didn't show significant differences between the three groups compared (Kruskal-Wallis test) probably because the asymptomatic group of patients was very small. Further, with these data we consider inform about implication of cofactor in food allergy only in selected cases and not routinely.

TP0928 | Epidemiology of food allergy in Czech Republic, final results of dafall registry

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Background: Food allergy occurence has significantly risen in recent two decades. The prevalence has reached 6-8% in children and 3-4% in adults. There are some geographical differences in incidence of types of food allergy as well as in the most common triggers of food induced anaphylaxis. Only limited evidence is available regarding epidemiology of food allergy in the Czech republic. The aim of the present study was to provide data describing patients suffering from food allergy in the Czech republic.

Method: DAFALL- Database of Food Allergies - was an electronic registry founded in October 2014, collecting data since January

2015 till December 2017. Patients with newly diagnosed food allergy were included. Most common triggers of food reactions, severity of reactions, threshold doses, processing of food allergens, laboratory test results including component resolved diagnosis and skin prick tests as well as allergology history of the patients were evaluated.

Results: During the 36 months period, 1742 patients were enrolled from 34 collaborating allergology outpatient clinics, most of them children under age of 6 years (n = 840), 26% children aged 6-18 years (n = 455) and 447 adults. In children under 1 year of age, cow′s milk was the most frequent food allergen. In 86% of cases, first symptoms of milk allergy were recorded below the age of 7 months and in 60% of cases noted in fully breast-fed kids. About 60% of milk reactions were non-IgE mediated, with no prove of any positivity in skin prick tests and/or specific IgE against milk. Most common triggers of allergy in children between 1 and 6 years of age were milk, egg, tree nuts, peanut and fruits. In patients older than 6 years, significant allergens were tree nuts (hazelnut, walnut, almond), fruits (apple, peach, kiwi), vegetables (carrot, potato, tomato), peanut and seeds (sesame seed and poppy seed). Relatively low occurence of allergy to fish, shellfish and soy in all age groups was registered in contrary to high number of patients reacting to seeds. Most common triggers of food induced anaphylaxis were peanut, milk, seeds and cashew nuts, which seems to be one of the allergens with highly rising prevalence also in Czech patients.

Conclusion: DAFALL was the first project in the Czech republic describing relevant data on food allergy in the Czech population. We have found some interesting differences specific for Czech food allergic patients.

TP0929 | Clinical case of familial food intolerance

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Case report: Two children with complaints about the development of systemic reactions after consuming meat (M., born in 2013) and fish (D., born in 2009).

M. at the age of 5 months after the first attempt to introduce meat (beef) in a small amount (5 mg) had a reaction: anxiety, repeating vomiting, pallor of the skin appeared 30 minutes after. The same symptoms were observed when trying to introduce turkey, rabbit. Next meat introduction was at the age of 1 year. 30 minutes after - weakness, pallor of the skin, repeating vomiting for 3 hours. The infectious nature of the observed symptoms was excluded. A strict diet with the exception of meat was prescribed.

D.: the symptoms of intolerance to fish manifested in 1-1.5 years, during the second attempt to introduce fish. After 15 minutes – vomiting within a few hours. Emergency care was provided. A strict diet with the exception of fish was prescribed.

Examination:: M.: Blood test – normal. Ultrasound examination in 2015: echo signs of reactive changes of liver and pancreas. Folded gallbladder, the enlargement of the spleen and mesenteric lymph nodes. Ultrasound examination in 2018: moderate enlargement of the liver, spleen, mesenteric lymph nodes.

Skin prick tests with diagnostic allergens (domestic, epidermal, pollen, food), prick-prick tests with boiled chicken, pork, turkey, rabbit, lamb, beef, veal were negative. ISAC: sensitization to the Feld1 8.7 ISU-E (medium/high level) was detected.

A blind placebo-controlled test with beef was negative.

D.: Blood test – normal. Ultrasound examination in 2015: echo signs of reactive changes of liver and pancreas. Folded gallbladder, the enlargement of the mesenteric lymph nodes. Ultrasound examination in 2018: Folded gallbladder, moderate enlargement of the liver, mesenteric lymph nodes. sIgE to mixed fish: cod, herring, mackerel, flounder – negative. Skin prick tests with diagnostic allergens (domestic, epidermal, pollen, food), prick-prick tests with boiled cod, trout, salmon, shrimp, squid, mussels were negative. ISAC: negative.

A blind placebo-controlled test with cod was negative.

Conclusion: Thus, it can be assumed that the development of food intolerance reactions in these patients is not related to the IgE-dependent mechanism. Perhaps we can see the involvement of genetic factors that ensure the normal digestion and absorption of food substrate or other reasons that require clarification.

TP0930 | Potential allergic reaction in patients with food allergy taking complementary and alternative medicine (CAM) containing food ingredients

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Background: Complementary and alternative medicine (CAM) is usually considered to be without any allergic and adverse reaction

Method: Visits were made to pharmacies in South East Asia (Bangkok, Thailand, and Hong Kong and Macau, China). Some CAM were found to have ingredients containing food products.

Results: Three CAM were found to contain food ingredients including dairy, wheat, soy, tomato and pumpkin seed. Patients with allergy to specific food products may have potential allergic reaction upon taking them unintentionally.

(A) Ryukakusan nodo sukkiri ame stock
(Highly concentrated throat lozenge)
A product of Japan

Ingredients: corn syrup, skim milk powder, margarine and others (“contains of milk; may contain of wheat”)

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(B) LIVER PROTECT

A product of Australia

Ingredients: soy lecithin, soya oil and others

"This product contains soy ingredients."

(C) Prostate Care

A product of New Zealand

Ingredients: tomato extract, pumpkin seed and others

Conclusion: Potential allergic reaction may occur in patients with food allergy taking CAM containing specific food ingredients. Careful examination of the ingredients of CAM is important. Patients with serious food allergy should read food labels carefully and also the ingredients in CAM which may continue food oviducts.

SUNDAY, 2 JUNE 2019
TPS 18
UPDATE ON IMMUNODEFICIENCY

TP0931 | New ellagitannins from geranium sanguineum and punica granatum: Anti-HIV activity and immunosuppressive effect on dendritic cells

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Background: Ellagitannins (ETs) are a diverse class of hydrolyzable tannins widely distributed in the plants. Ellagitannins contain polyphenolic units formed primarily from the oxidative linkage of galloyl groups in 1,2,3,4,6-pentagalloyl glucose. The objective of this study was to assess the anti-HIV activity of ellagitannins from the leaves of *Geranium sanguineum* afforded 1-O-trigalloil-2,3,4,6-bis-O-hexahydroxydifenoil-β-D-glucopyranose (trivial name ET-Gs) and from the peel of *Punica granatum* afforded 1-O-galloil-3,5-bis-O-hexahydroxydifenoil-β-D-glucopyranose (trivial name ET-Pg), isolated for the first time from this plant species. We also evaluated the immunosuppressive effects induced by ET-Gs and ET-Pg treatment in human dendritic cells (DCs), which play a critical role in the initial immune response on transmission dynamics for sexually transmitted infections.

Method: The evaluation of anti-HIV efficacy of new ETs was performed using HIV-1 BRU or HIV-1 MvP-899 and different cell targets (TZM-bl, MT-4). HIV-1 replication was detected by measuring p24 antigen in the culture supernatant. The cytotoxicity effect was determined using MTT assay. The immunomodulatory effects induced by ET-Gs and ET-Pg on DCs were measured by cytokine production, cell differentiation, and cell viability.

Results: ET-Gs and ET-Pg showed pronounced anti-HIV activity in a dose-dependent manner: 50% suppression of HIV replication was achieved at concentrations of 0.11 μg/mL and 0.10 μg/mL, respectively. ET-Gs and ET-Pg showed significant down-regulation of the expression of cell surface molecules, CD1a and CD83, suggesting the inhibition of DC differentiation and maturation. ET-Gs and ET-Pg also markedly suppressed the production of inflammatory cytokines, such as IL-1β, IL-6, and TNF-α in a dose-dependent manner. Since HIV has evolved ways to exploit DCs to facilitate viral dissemination and to evade antiviral immunity, identified properties of new ETs are very significant.

Conclusion: ET-Gs and ET-Pg hold significant promise as safe and efficacious drugs for the treatment of HIV infection. New ETs may be used as a immunoactive reagents anti-HIV microbicides.

TP0932 | Secondary immune deficiency syndrome in combatants

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Background: Objective: to study the severity of immune dysfunction in chronic stress in combatants.

Method: Examined 75 retired officers, participants of special operations. The mean age was 58.8 ± 2.46 years. The main group (n = 38) of patients with clinical manifestations of secondary immune dysfunction was identified. The control group (n = 40) consisted of retired officers who did not participate in special operations. Immune status was assessed by expression of CD 3 + , CD 4 + , CD 16 + , CD 19 + , CD 4 + , CD25 + Foxp3, content granzyme in CD 8 + , NK cells in immunofluorescence test on flow cytometer Cytomics FC 500 (Becman Coulter, USA) using appropriate monoclonal antibodies.

Results: Results: in the main group expression of late activation markers (CD3 + HLA DR + 4.77 ± 0.7% in the study group and 3.81 ± 0.72% in the control group, $P \leq 0.05$) and readiness to apoptosis T-lymphocytes (CD3 + CD95 + 4.6 ± 0.3% and 2.85 ± 0.2%, respectively, $P \leq 0.05$) were increased, identified activation of the functional reserve of cytotoxic T-lymphocytes (CD8 + HLA DR + 3.9 ± 0.3% in the study group and 2.02 ± 0.2 0.5% in the control group, $P \leq 0.05$). In humoral link the tendency to activation of maturation of b-lymphocytes and increase of immunoglobulin of class A was revealed. The weakening of the adaptive capacity of neutrophils is manifested by the inhibition of their activity in patients of the main group.

Conclusion: The manifestation of immune dysfunction in combatants in the remote period of hostilities develops against the background of structural and functional changes in the innate and adaptive parts of the immune system.

TP0933 | A case of severe combined immunodeficiency misdiagnosed as cystic fibrosis

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Case report:

Background: Severe combined immunodeficiency (SCID) is a pediatric emergency. The only curative treatment is hematopoietic stem cell transplantation (HSCT). Herein, we presented a case of SCID threatened as cystic fibrosis at the external center due to recurrent lung infection and malnutrition.

Case report: An 11-months-old boy referred to our hospital because of respiratory insufficiency and requiring intensive care unit, while he is being followed with the diagnosis of cystic fibrosis. It was learned that he was healthy until 4 months. He had been hospitalized 4 times for lung infections between 4-8 months. At the age of 9 months, cystic fibrosis was considered due to malnutrition, lower respiratory tract infection, lack of improvement in her clinic under multiple antibiotic treatment, hypoalbuminemia and elevated liver enzymes. Creon treatment had been started. He was admitted to our hospital because of respiratory failure and need for intensive care. In our first visit, his physical examination was revealed respiratory failure with crepitant rales, moniliasis and growth retardation. Chest X-ray showed interstitial infiltration in bilateral lung fields with an absent thymic shadow. Laboratory investigations revealed lymphopenia with agammaglobulinemi immunoglobulin values. Intravenous immunoglobulin treatment was initiated with fluconazole and bactrim prophylaxis. Flow cytometry revealed a diagnosis of T (-) B (-) NK (+) SCID.

Conclusion: Severe combined immunodeficiency is a pediatric emergency. It is known that the success of HSCT which is the only curative treatment is higher if diagnosed without developing organ damage and malnutrition. In our case, although there were many signs of immunodeficiency such as lung infections which could not be easily treated, growth retardation and lymphopenia, immunodeficiency was not considered. Immunodeficiency should be considered primarily in patients with recurrent infections. In addition, lymphocyte counts should always be taken into account in the complete blood count.

TP0934 | Hyper IgE syndrome due To DOCK-8 mutation

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Case report:

Background: DOCK8 deficiency is an autosomal recessive combined immunodeficiency syndrome associated with elevated IgE, recurrent sinopulmonary and cutaneous viral infections, atopy, and malignancies. It is the most common autosomal recessive hyper IgE syndromes with clinical trial of eczema, infections and elevated IgE levels. Here, we report a case of DOCK-8 deficiency admitted to our outpatient clinic due to atopic dermatitis.

Case report: An 11-months-old boy was admitted to our outpatient clinic because of eczematous skin lesions. Physical examination revealed diffuse itchy eczematous skin lesions on the most part of the body and skin abscess on the scalp. He had been followed-up with diagnosis of atopic dermatitis since 2 months of age at the external center. In his previous history he had one more skin abscess which was healed spontaneously with draining. He had had a pneumonia and an otitis once. He had received antibiotics for these infections. There were no lymphopenia and neutropenia in the laboratory tests. The eosinophilia was 11.5% and 2100/mm3. Immunoglobulin levels were normal for age. The IgE value was > 2000 IU/L. Flow analysis revealed CD4 lymphopenia. DOCK-8 mutation was studied in the patient and wide deletion was detected in DOCK-8 gene. In his follow-up, he had had eczema herpeticum 1 time and acyclovir treatment had received. Intravenous immunoglobulin treatment was started at 400 mg/kg dose for every 4 weeks. Bactrim and flucanazole prophylaxis were started. The patient who underwent HSCT from his fully compatible sibling is followed up in the 1st year after the HSCT and without any complaint.

Conclusion: Hyper IgE syndrome due to DOCK-8 deficiency is a combined immune deficiency. Patients who admitted with atopic dermatitis, elevated IgE levels and infections should be evaluated for hyper IgE syndromes. All physicians including pediatricians and dermatologists should be familiar with this clinical entity.

TP0935 | Common variable immune deficiency and allergic disorders: Incidence rate, clinical characteristics and diagnosis

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Background: Common variable immune deficiency (CVID) is known to be associated with immune dysregulation. However, studies focusing on the prevalence of atopy in CVID patients are scarce. In this study, we will define the incidence rate of allergy in CVID patients and characterize clinical and laboratory features

Method: Adult patients (≥18 years) diagnosed with CVID in the period of 2002-2017 at Hadassah-Hebrew University Medical Center and Shaarei Zedek Medical Center; Jerusalem, Israel, were enrolled in the study. The study is comprised of chart reviews, telephone survey and physical examination including skin allergen testing, complete blood count, serum IgE levels and pulmonary function tests.

Results: 65 CVID patients were identified in the study period. 24 patients were excluded from the study. Telephone surveys were conducted in 41 patients (18 males). Most patients are Jews (95%). Medical background included autoimmunity in 20/41 (48%).. Increased prevalence of allergy among CVID patients, in comparison to the general population, was notable. Most CVID patients (80%, 20/25) expressed allergic symptoms or diagnosis despite low/ undetectable IgE levels. This included: asthma 7 (35%), allergic conjunctivitis 9 (45%), allergic rhinitis 15 (75%) and atopic dermatitis 2 (10%) patients. Patients are summoned to the immunological clinic for physical examination, skin allergen testing, complete blood count, serum IgE levels and pulmonary function tests.

Conclusion: Based on chart reviews and telephone survey, atopy is prevalent in CVID patients. It seems that CVID patients are often under-diagnosed and untreated for allergic diseases. This study will promote awareness for allergic disorders diagnosis among CVID patients and will enable early diagnosis, comprehend mechanism of allergy and offer targeted treatment accordingly.

TP0936 | Laboratory markers of allergic diseases among patients with common variable immunodeficiency (CVID)

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Background: Common variable immunodeficiency (CVID) is a primary immunodeficiency disorder characterized by impaired antibody production and low levels of IgG, IgA and/or IgM. Typical clinical features are proneness to bacterial infections, autoimmune diseases, granuloma formation and chronic lung disease. Suspicious allergic symptoms are referred by some patients with CVID but diagnostic tests (skin prick test or specific IgE) of allergic diseases are usually negative.

Method: A retrospective analysis of medical records of 40 patients with CVID (16 males, 24 females, aged 20 - 84 years) was performed. We focused on laboratory markers of allergic diseases such as total and specific IgE, markers of eosinophilic inflammation - eosinophil cationic protein (ECP) and fraction of exhaled nitric oxide (FeNO) and pulmonary function tests (FVC, FEV1 and FEV1/FVC ratio).

Results: No patient had elevation of total IgE levels. Specific IgE antibodies against suspicious allergens determined in 10 patients with allergic symptoms (rhinoconjunctivitis, asthmatic symptoms or drug hypersensitivity reaction) were negative. Elevation of ECP above upper limit of normal was recorded in 6/40 patients (15.0%) but the elevation was mild (reference range: 0 – 24 ng/mL, highest value: 26.8 ng/mL) in all cases. We recorded elevation of FeNO above 25 ppb in 7/16 patients (43.7%), but only in 1/16 patient (6.2%) the elevation was above 50 ppb. However, this patient had no allergic or asthmatic symptoms and had no abnormalities in pulmonary function tests and ECP. In our group, we observed 4/37 patients (10.8%) with FVC below 80 percent predicted, 6/37 patients (16.2%) with FEV1 below 80 percent predicted and 3/37 patients (8.1%) with decreased FEV1/FVC ratio below 0.7; however, all these patients had ECP within normal range.

Conclusion: Diagnosis of allergic diseases in patients with CVID is challenging because laboratory parameters (total or specific IgE) are negative in most of the cases. Although some patients suffer from suspicious symptoms of allergy, our results did not show significant markers of type-one hypersensitivity. Pathogenesis of these symptoms in patients with CVID remains unknown but probably is not mediated by IgE or by eosinophilic inflammation.

TP0937 | Consequences of non compliance in patient with common variable immunodeficiency disorder (CVID)

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Case report:

Introduction: Common variable immunodeficiency disorder (CVID) is a heterogenous group of primary immunodeficiencies. Onset of illness is typically in adults; however, children above 2 years of age may be also affected. Immunodeficiency is demonstrated by a sudden decrease of serum concentration of immunoglobulins associated with variable T or B cells abnormalities. The absence of immunoglobulins leads to severe bacterial, fungal or parasitic infections and higher risk of autoimmunity or malignancies.

Case report: We report the case of 44 years old man being diagnosed -as a CVID in 30 years of age after an occurrence of recurrent pneumonias and presence of bronchiectasis requiring thoracic

surgery. Patient's father died in the age of 49 years for lung cancer. Immunological examination has confirmed severe deficiency in humoral immunity, particularly a dramatic decrease of serum immunoglobulins. After a consequent intravenous immunoglobin (IVIG) substitution, immunoglobulin levels normalized and frequency of infections decreased to allow switching to subcutaneous (SCIG) home therapy. After 3 years, gastrointestinal symptoms appeared as a sign of CVID enteropathy. Two years later, patient's complaints regarding local side effect after SCIG administration led to a temporary switch back to IVIG. Regardless the intensive treatment of CVID enteropathy with enteral budesonide and increased doses of IVIG, asthenia and frequency of diarrheas further progressed. At that time, the patient decided to discontinue our therapy and started alternative forms of treatment. Following the period of more than one year without IVIG substitution, he underwent severe septic enterocolitis (Clostridium difficile) requiring 3 weeks of hospitalization, recurrent severe maxillar sinusitis with antibiotic therapy, serious pneumonia with fluidothorax and continuously suffered from persistent purulent rhinitis. When he returned to our outpatient clinic, serum IgG was undetectable. After a careful resubstitution by IVIG 5 g/weekly, diluted by 5% of glucose, premedicated with paracetamol for 4 months, levels of IgG normalized, however IgM and IgA remained undetectable. The clinical status of the patient is relatively stable and the rate of infections decreased to a normal range.

Conclusion: CVID is a chronic illness commonly affecting people in a productive age who do not always accept the long life treatment. In this respect, closer cooperation with psychologist or psychotherapist might be helpful.

TP0939 | Phenotypic differences between selective IgA deficiency and other primary immunodeficiencies

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Background: Primary immunodeficiencies are a widely heterogeneous group of congenital diseases caused by quantitative and/or functional alterations of mechanisms involved in the immune response that increase the susceptibility to allergy, infections, autoimmune processes and cancer. There is no detailed information in our country of its clinical spectrum that allows its correct management. Objective: To compare the phenotypic expression of patients with selective IgA deficiency with other primary immunodeficiencies.

Method: An observational and analytical epidemiological study was conducted in 124 patients from the province of Pinar del Rio who had received a clinical diagnosis of primary immunodeficiency according to the current classification.

Results: The phenotype/clinical spectrum was shown in patients diagnosed with IDPs. Patients who belong to the group of other IDPs are more likely to present the set of clinical phenotypes, which facilitates their diagnosis.

Conclusion: There are phenotypic differences between the selective IgA deficiency and other primary immunodeficiencies that allow to guide a better diagnosis and prognosis suspicion for these entities.

TP0940 | Chediak–Higashi syndrome: Lessons from a single-centre case series

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Background: Chediak-Higashi Syndrome (CHS) is a rare and potentially fatal autosomal recessive disease characterized by frequent bacterial infections, bleeding tendency, oculocutaneous albinism, photosensitivity and progressive neurologic dysfunction. Owing to the rarity of this condition, the objective of this study was to describe patients with CHS.

Method: Retrospective evaluation of patients followed in a paediatric tertiary center of Allergy and Immunology of São Paulo, Brazil, between 1986 and 2018 with a confirmed diagnosis of CHS. Data were obtained from medical records. Demographic aspects, family history, clinical findings, laboratory data, diagnosis, treatment and outcome were described.

Results: A total of 14 patients (five male) were included. Clinical manifestations were first recognized at a median age of 2 months (at birth – 20 months). Median age at diagnosis was 1.7 years (0-5 years). All patients had recurrent infections. Albinism was present in thirteen patients and silvery or light hair was present in fourteen. Seven patients developed hemophagocytic lymphohistiocytosis (HLH), the median age at the diagnosis of HLH was 5.7 years (2.6-6.7 years) and the median interval between the diagnosis of CHS and HLH was 3.3 years (0-5 years). Four of the most recently diagnosed patients underwent bone marrow transplantation (BMT). Nine patients are deceased, and one lost follow-up. The median age of death was 6.7 years (3.8-22 years). Five patients died of HLH, one of lymphoma, and three of infection. All the patients who had HLH before the year of 2000 died of HLH. The two more recently diagnosed patients with HLH were able to cure the HLH, although they died of other causes. Four patients are alive, three of them after successful BMT.

Conclusion: Thirty years of follow up showed an improvement on the prognosis in patients with CHS. The better understanding of the underlying biological mechanisms of HLH allowed the

standardization of management protocols, resulting in a survival improvement. BMT is the only treatment that can change CHS prognosis, which emphasizes the need for early identification of the disease.

TP0941 | Positive clinical and immunological effects of combine interferon- and immunomodulatory therapy in patients with atypical chronic viral-bacterial co-infections

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Background: The atypical chronic viral-bacterial co-infections are often associated with multi-syndromes and different clinical masks that are clinical criteria of immunodeficiencies. It should be emphasized that in these comorbid diseases among viral infections are often observed recurrent acute respiratory viral (ARVI), various herpesvirus infections (HV), and among bacterial - chronic tonsillopharyngitis with frequent relapses. At the same time, the methods of treatment of those diseases are imperfect.

Method: We had studied 35 adult patients suffering from different recurrent infections of respiratory tract (RIRT) of viral-bacterial etiology. Among them herpes viral infections (HVI) in different combination were observed in 100% of cases. Dominant combinations were: EBV+CMV и EBV+CMV+HHV1- 14%; EBV+CMV+HHV 3-11%; EBV+HHV 6 - 9%; CMV+HHV 6 - 9% and etc. The prevailing clinical symptoms were: throat transient pain -91.4%; chronic fatigue syndrome (CFS) - 32%; subfebrile temperature 34.2%; cognitive disaster- 15%. The diagnostic complex included: the complaints, anamnestic and clinical features, immunological (the main antiviral mechanisms and the interferon system) investigations. HVI were tested by PCR and serodiagnostic methods.

Results: Secondary combine immunodeficiencies were detected in all patients: Induced production of INFα and INFγ were decreased in 97% of cases. Combine defects of immune system were detected in 97.6% patients: decrease the number of Tctl in 81.6, Th- 49.2%, NK -31.4%, neutrophils (NG) - in 80.4% of cases. The program of combine IFN- and immunomodulatory therapy was created based on the installed immunopathogenesis of co-infections. For restore IFN system suppositories of the recombinant INFα2 in combination with antioxidants were used, with gradually decreasing doses, course - 4.5 months. Immunomodulatory therapy was next: for restoration of NG- glucosaminylmuramyldipeptide (GMDP) 3 ten days courses every months were used, for restoration Tctl and NK - 3 ten days courses of inosine pranobex (IP). The course duration of combine IFN- and immunomodulatory therapy was 4.5 month.

Conclusion: The obtain data had shown that created program of IFN- and immunomodulatory therapy had demonstrated positive clinical and immunological effects in patients with atypical chronic viral-bacterial co-infections in 100% of cases: regression of all clinical symptoms and restoration of impaired IFN- and immune systems.

TP0947 | Normal NFKB2 gene by sanger sequencing in a patient with hypogammaglobulinaemia, alopecia and central adrenal insufficiency

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Background: Hypogammaglobulinaemia, recurrent infections, central adrenal insufficiency and alopecia are features of an Inborn Error of Immunity Syndrome caused by a defect in Nuclear factor kappa-B subunit 2 (*NFKB2*) gene. Typically this is due to a heterozygous mutation of exon 23 affecting the amino acid sequence around critical serine residues 866 and 870 resulting in non-processable NFKB2 protein (Lui et al. 2014). We postulated such a defect in a patient with these clinical features.

Method: We performed a review of the clinical data and *NFKB2* gene sequencing (Sanger) of exon 23.

Results: A 19-year-old Asian male patient diagnosed with panhypogammaglobulinaemia at 3 years of age subsequently developed central adrenal insufficiency, alopecia areata and chronic rhinosinusitis. A core needle biopsy of the liver, performed to investigate deranged liver function tests, demonstrated perisinusoidal fibrosis with perivenular fibrosis and patchy nodular regenerative hyperplasia (NRH)-like change and cholangitic features. He is currently managed on intravenous immunoglobulin replacement therapy every three weeks, receives aminoglycoside nebulisers for the treatment of chronic infection with *Pseudomonas aeruginosa* and hydrocortisone replacement therapy. DNA Sanger sequencing of exon 23 of the NFKB2 gene was normal.

Conclusion: In a patient with the classical clinical manifestations of non-processable NFKB2 syndrome, no mutation of exon 23 of the gene was identified. This suggests other heritable or acquired factors could be involved in the aetiology of this condition.

TP0948 | Humoral and cellular immune decline in a patient with CDC42 deficiency

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Case report:

Background: Single allele mutations in the Cell Division Control protein 42 homolog (CDC42) gene have been recently described as causing Takenouchi-Kosaki syndrome. Patients can present with diverse manifestations including mild thrombocytopenia associated with large platelets size, moderate to severe developmental delay, growth retardation, facial dysmorphism as well as other neurodevelopmental and hematological anomalies. Little is known about immunologic manifestations of CDC42 deficiency. As this protein closely interacts with the Wiskott-Aldrich Syndrome Protein, there is a possibility that CDC42 deficiency may have an impact on immune system, particularly in patients who present with frequent infections or autoimmunity.

Method: Detailed humoral, cellular and innate immune evaluations were performed in a female patient diagnosed with a Tyr64Cys mutation in CDC42 gene followed for 13 years by the immunology service at a single centre.

Results: The 16-year old female patient suffered at early age from recurrent pneumonia, otitis media and bacteremia, which eventually resolved at 10 years of age, concordant with the initiation of amoxicillin prophylaxis. In addition, the patient had frequent recurrent upper respiratory tract infections caused by variety of viruses that resolved without medical interventions. Immune evaluations (table 1) demonstrated inability to maintain antibody responses to T-cell dependent and independent antigens. The patient also showed gradual decline in the number of CD19 + B cells as well as CD4 + and CD8 + T cells. T cell diversity was restricted, naïve T cells were markedly reduced and the response of the patient's T cells to phytohemagglutinin (PHA) stimulation was depressed; however, no opportunistic infections were observed. Natural Killer cells number and function remained normal.

Conclusions: Persistent and progressive decline in T and B cells numbers and functions might be associated with CDC42 deficiency. We suggest close monitoring of humeral and cellular immunity in affected patients, particularly among those with frequent infections.

Age (year)	CD19 cells/μl	CD4 cells/μl	CD8 cells/μl	CD3-CD16 + CD56 + cells/μl	T-cell response to phytohemagglutinin (PHA)
5	415	531	251	446	-
7	157	347	274	196	-
10	184	292	225	314	5% (low)
13	150 (low)	258 (low)	300	248	-
16	76 (low)	162 (low)	132 (low)	176	23% (low)

SUNDAY, 2 JUNE 2019
TPS 19
INSECT VENOM ALLERGY: CLINICAL ASPECTS

TP0949 | Can low total IgE levels be a risk factor for severe anaphylaxis in venom hypersensitive adult patients?

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Background: Venom induced hypersensitivity reactions (HRs) are one of the most common causes of anaphylaxis in adult patients. The aim of the study was to investigate the potential risk factors including demographic, clinical and laboratory findings of the patients that may affect the severity of a sting reaction.

Method: 187 venom allergic patients who were admitted to our adult allergy clinic between 2014 and 2019 were included in the study. Severity of sting reactions was graded according to the Mueller classification. Demographic and clinical characteristics as well as in vivo and in vitro diagnostic tests, serum basal tryptase and total IgE levels were compared according to the severity of the reactions.

Results: Culprit insects in the history were bee, wasp and both in 99, 50 and 10 patients, respectively and 28 patients were unaware of the insect type. Types of reactions in the history were large local reactions (n = 13) and systemic HRs (n = 174) including anaphylaxis (n = 149), urticaria (n = 13), angioedema (n = 4) and both urticaria and angioedema (n = 8). 31 patients experienced syncope or presyncope without any skin lesions. 14 patients were beekeepers. Asthma, allergic rhinitis, food allergy, chronic urticaria and drug allergy were seen in 5.7%, 13.9%, 3.6%, 9.9% and 14.5%, respectively. 40.6% of the patients had comorbidities other than atopic diseases including hypertension (21.3%), diabetes (15.7%) and coronary artery disease (13.2%). 36.9% of the patients were using concomitantly drugs comprising ACE inhibitors and/or angiotensin receptor blockers (17.6%), beta blockers (15.3%) and anti-diabetics (15.7%). The frequencies of grade 1, 2, 3 and 4 reactions were 13.4%, 9.1%, 23.5% and 46.5% respectively. All patients with systemic mastocytosis (n = 7) experienced grade 4 reactions (P = 0.005) and grade 4 reactions were more common among males than females (P = 0.03). In the patients who experienced grade 3 or 4 reactions had less frequently chronic urticaria and allergic rhinitis and lower total IgE levels than the patients with grade 1 or 2 reactions (P = 0.003; P = 0.038; P = 0.035, respectively).

Conclusion: In venom hypersensitive patients having chronic urticaria, allergic rhinitis and higher total IgE levels could be protective against severe reactions which need to be confirmed with studies in other adult populations.

TP0950 | Could the development of systemic reactions during venom immunotherapy be predicted?

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Background: The aim of the study was to clarify the factors that might predict the incidence and development of systemic reaction (SR) during venom immunotherapy (VIT).

Method: A total number of 113 patients who underwent VIT for the last 5 years were examined retrospectively. The Müller Scale was used for the index reaction (IR) and "SCIT Systemic Reaction Grading System" for the SR classification. The relationship between demographic characteristics, IR intensity, time until initiation of VIT, levels of TIgE, TIgE/SIgE, tryptase, vitamin D, eosinophil-basophil values, presence of local reaction (LR) and development of SR were investigated.

Results: The median intensity of IR is 3.31 ± 0.6 (1-4) in 113 (59 K, 54 E) adult patients. The type of applied VIT was *Apis mellifera* in 73.6% and vespula in 26.3% of the patients. Of the patients, 60 (77.9%) had aeroallergen sensitivity, 17 (15.4%) had asthma, and 32 (28.4%) had hypertension. Twenty-five SRs were observed in 17 patients. The vast majority of SRs was grade 2 (11 patients-64.7%). Sixty-four percent of SR was developed in build-up phase. Recurrent LRs was observed in both build-up phase (3 patients) and maintenance phase (8 patients). SR was more common in female (P = 0.03) and younger patients (P = 0.4). In patients with SR, TIgE, T/sIgE and basophil counts were significantly different (P = 0.009, P = 0.01, P = 0.02). There was no significant correlation between IR intensity, VIT type, time until VIT, presence of asthma, antihypertensive drug use, presence of LR and tryptase level.

Conclusion: SR was more common in female and young patients during VIT, and TIgE, T/SIgE and basophil levels could be predictor in SR development.

TP0951 | Sensitization to Api M 1, Api M 2, and Api M 4 in Japanese beekeepers who had experienced systemic reactions to honeybee stings

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Background: The major allergen components of honeybee (HB) venom are phospholipase A2 (Api m 1), hyaluronidase (Api m 2), and melittin (Api m 4).IgE antibodies specific(s) to phospholipase A2, hyaluronidase, and melittin bind to recombinant (r)Api m 1, rApi m 2, and rApi m 4, respectively, and show increased test specificity due to the lack of carbohydrate determinants in the recombinant protein. However, the significance of measuring the levels of sIgE to these allergen components is not known. In this study, we analyzed sensitization to Api m 1, Api m 2, and Api m 4 in Japanese beekeepers who had experienced systemic reactions (SRs) to HB stings.

Method: The participants comprised 121 beekeepers in Japan. Of the beekeepers, 34 who had experienced an SR to a HB sting were analyzed in this study. All participants underwent a medical examination including an interview with an allergist and peripheral blood tests were performed on the day of the examination.

Results: sIgE positivity to HB venom, rApi m 1, rApi m 2, and sApi m 4 was identified in 32 (94.1%), 31 (91.2%), 33 (97.1%), and 18 (52.9%) beekeepers, respectively. Double positivity to rApi m 1 and rApi m 2 was found in 30 individuals (88.3%). The combination of rApi m 1 and rApi m 2 resulted in the sensitivity increasing from 94.1% (32/34)to 100% (34/34).

Conclusion: Combination measurement of sIgE to rApi m 1 and rApi m 2 may improve the sensitivity for HB venom allergy detection.

TP0952 | Diagnosis of hymenoptera venom allergy in Russia

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Background: Clinically Hymenoptera venom Allergy (HVA) is characterized by a particular severity and rapid development of life-threatening symptoms after a bite. In Russia, there are no registered therapeutic and diagnostic allergens of Hymenoptera insects (HI) for skin testing, as a result of which laboratory diagnostics takes a leading role. The main methods of diagnosis of HVA are ELISA, chemiluminescent and fluorescence tests. These methods are aimed at identifying specific IgE (sIgE) to the venom allergens of HI. However, they do not allow to identify another type of reactivity to the venom, namely non-IgE-mediated reactions, which are characterized by the absence of sIgE, but the involvement of target cells in the hypersensitivity process, the liberalization of Allergy mediators and the subsequent implementation of their action on the organs, and occur in about 5-30% of cases. To assess the resistance of the membrane of effector cells to the effects allergens of HI, it is advisable to determine the level of allocated mediators of Allergy and expression of molecules of activation and degranulation on the surface of these cells.

Method: 55 patients with anamnestic data on the development of hyperergic reactions to honeybee sting were examined. The blood and serum of all patients were studied by immunological methods for the content of sIgE to the venom of HI, as well as the expression of degranulation CD63 and activation molecules CD203c by flow cytometry.

Results: In the study of patient sera by ELISA and its modifications with allergen extracts or allergen components, the presence of positive sIgE was revealed in 39 (71%, n = 55) patients. During the BAT, expression of CD63 molecules and significant expression of CD203c under the action of allergens of HI were noted in all 39 patients. Also, during the examination in 16 (29%, n = 55) patients with a positive history, when TAB with stimulating doses of venom of HI in the expression of CD63 is not revealed, but revealed a moderate increase in expression of CD203c. These patients are regarded as a group with a non-IgE-mediated HVA.

Conclusion: Allergy to the venom of Hymenoptera reduces the quality of life and causes serious socio-economic problems, timely and correct diagnosis contributes to the appointment of adequate pathogenetic therapy. The conducted researches show the necessity of wide introduction of methods of flow cytometry in laboratory diagnostics in Russia.

TP0953 | Is the clinical manifestation of anaphylaxis in children influenced by the trigger of reaction?

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Background: Anaphylaxis remains an important clinical issue. The aim of the study was to indicate the triggers of anaphylaxis and their influence on clinical characteristics of patients treated in the tertiary pediatric center.

Method: Validated structured on-line questionnaire to collect data concerning the medical history of children admitted to diagnostics and/or intervention due to episode of anaphylaxis in

2015-2017 years. Study was conducted within cooperation with European Anaphylaxis Registry.

Results: Study group: 86 children (60 boys, 69.8%) aged 5 months – 17 years. The most frequent triggers of anaphylaxis were: insect venom (n = 43, 50%), food (n = 30, 35%), drugs/AIT (n = 7, 8%). Clinical manifestation presented as: dermal (n = 85, 99%), gastro-intestinal (GI) (n = 49, 57%), respiratory (n = 81, 94%), cardiovascular (n = 64, 74%) symptoms. Cardiovascular symptoms concerned all children with anaphylaxis triggered by drug, almost all triggered by venom and half triggered by food (P = 0.005). GI symptoms concerned ¾ of children with drug and food allergy, and less than half allergic to venom (P = 0.014). Mean age of children with GI symptoms was lower (m = 7.4 ± 4. years) than those without (m = 9.6 ± 4.9 years, P = 0.014). Children with venom allergy were older (m = 9.6 ± 4.0 years) than these with food allergy (m = 6.2 ± 5.2 years, P = 0.042). Life-threatening symptoms occurred in 20 children (m = 9.6 years ± 3.8) (11 boys), presenting as fall of the blood pressure (n = 19, 22%), and loss of consciousness (n = 5.5, 6%), triggered by: venom (65%), food (20%) and drugs (15%). In almost half of children (n = 40, 47%) the first symptoms of anaphylactic shock revealed up to 10 minutes since exposure to causal trigger. Prevalence of allergic rhinitis was higher than the other atopic diseases, and it differed between groups of triggers (P = 0.022). Atopic dermatitis was present only in children with the food anaphylaxis (P = 0.013). Physical exercise occurred as the cofactor of venom anaphylaxis in comparison to the other triggers (P = 0.003).

Conclusion: Clinical manifestation of anaphylaxis in children is both trigger and age dependent. Dermal and respiratory symptoms are present in almost all children. Phenotype of the patient with food anaphylaxis presents as younger child with the mostly GI symptoms, while phenotype of the patient with venom anaphylaxis presents as older child with mostly cardiovascular symptoms. Physical exercise and atopy manifestation are associated with the trigger of anaphylaxis.

TP0954 | Intervention in anaphylaxis in children cohort—One center experience

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Background: Rapidity of medical intervention is crucial for the outcome of anaphylaxis. Aim of the study was to analyze the data on medical intervention in children admitted due to anaphylaxis to the tertiary pediatric center.

Method: Validated structured on-line questionnaire to collect data concerning the medical history of children admitted to diagnostics and/or intervention due to episode of anaphylaxis in 2015-2017 years. Study was conducted within cooperation with European Anaphylaxis Registry.

Results: Study group comprised of 86 children (60 boys, 69.8%) aged 5 months – 17 years. In 60.5% of the children the first line of medical intervention was provided by medical staff, in 26.7% it was provided in the first-line by non-medical person, while in the second-line by the medical staff. The least often intervention was provided only by non-medical person, being mainly the family member, while 2.3% of children have got no intervention. Overall in the first line of rescue treatment 30.7% of children was given adrenaline im. In 2% it was injected by non-medical person, while in 27% children by the medical staff. Five percent of children were given the second dose of adrenaline. In pre-medical intervention oral antihistamine drugs were the most frequent (81.3%) option of treatment. In medical intervention systemic glucocorticosteroids given by iv/im route were the most frequent (77.3%) option. In 34% of children it was at least second reaction to the same trigger. Children treated with adrenaline were older (mean m = 10.1 ± 4.6 years), in comparison to those not treated (m = 7.4 ± 4.6 years, P = 0.016). There was no difference in frequency of adrenaline intervention among children with food anaphylaxis in comparison to venom anaphylaxis group. Sixty seven (78%) patients required in-hospital treatment, including 4 (5%) children admitted to ICU. Directly after episode of anaphylaxis 33.7% of children got the prescription for adrenaline to self-administration. Later on, 12.8% of children were provided with this prescription by GP, while 54.7% of patients by allergology doctor. Almost 10% of children already possessed adrenaline for self-administration due to previous episode of anaphylaxis.

Conclusion: The most frequently the first line treatment of anaphylaxis is provided by the medical staff. Children treated with adrenaline were older. After anaphylaxis episode only 1/3 of patients was provided with the prescription for adrenaline to self-medication.

TP0955 | Evaluation of venom allergy, anaphylaxis and adrenaline auto-injector knowledge level in turkish beekeepers and their family members

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Background: Bee sting reactions can cause a wide clinical spectrum of symptoms ranging from local reactions to severe and life-threatening systemic anaphylactic reactions in sensitized individuals. The risk of severe reactions increases with recurrent bee sting exposures. Beekeepers and their family members are at an increased risk

of anaphylaxis. In this study, the aim is to investigate the prevalence of anaphylaxis and allergic diseases in beekeepers and their family members, and to evaluate the level of knowledge about anaphylaxis and its management.

Method: A questionnaire was administered to 69 beekeepers from different regions of Turkey. The participants were divided into two main groups according to knowing the terms anaphylaxis or allergic shock.

Results: The mean age of beekeepers was 48.4 ± 12 years and 82.6% of them are male. The median beekeeping duration was 20 (min-max:0-50) years. The participants knew the term 'anaphylaxis' and 'adrenalin auto-injector' at a rate of 55.1% (n = 38) and 30.4% (n = 21), respectively. The number of beekeepers, who knew the term anaphylaxis with a college degree was significantly higher than those with a high school or elementary school degree (P = 0.0001). In the group who knew the term anaphylaxis, the adrenaline auto-injector knowing rate was significantly higher (P = 0.004). Among the beekeepers, who did not know the term of anaphylaxis, 74.2% of them had an idea about the signs of anaphylaxis. The beekeepers had allergic disease at a rate of 40.6% (n = 28) and anaphylaxis at a rate of %8.7 (n = 6) in himself and/or in family members (Table 1).

Conclusion: Venom allergy is an occupational risk for beekeepers and their family members. Therefore, beekeepers and their family members should be informed about anaphylaxis and its treatment. We think that it is important to increase the awareness and the knowledge level of adrenalin auto-injector during both vocational training and outpatient clinic applications.

	Knows the terms anaphylaxis or allergic shock (n = 38)	Does not know the terms anaphylaxis or allergic shock (n = 31)	*P* value
Age (yr)	46.4 ± 12.6	50.9 ± 10.9	0.124
Sex			
Male	7 (18.4%)	5 (16.1%)	0.803
Female	31 (81.6%)	26 (83.9%)	
Beekeeping duration (yr)	27.4 (0-40)	33.1 (2-50)	0.199
Educational status			
Elementary school	3 (7.9%)	15 (48.4%)	0.000
High school	6 (15.8%)	6 (19.4%)	
University	29 (76.3%)	10 (32.3%)	
Did you hear adrenaline auto-injector?			
Yes	17 (44.7%)	4 (12.9%)	0.004
No	21 (55.3%)	27 (87.1%)	
Do you know the signs of anaphylaxis?			
Yes	34 (89.5%)	23 (74.2%)	0.096
No	4 (10.5%)	8 (25.8%)	
Concomitant allergic conditions			
Yes	16 (42.1%)	12 (38.7%)	
Himself	8 (21.1%)	8 (25.8%)	
Children	6 (15.8%)	5 (16.1%)	0.775
Wife	2 (5.3%)	3 (9.7%)	
Relatives	3 (7.9%)	1 (3.2%)	
No	22 (57.9%)	19 (61.3%)	
Allergic disease distribution			
Asthma	8 (21.1%)	5 (16.1%)	
Allergic rhinitis	9 (23.7%)	6 (19.4%)	
Drug allergy	4 (10.5%)	4 (12.9%)	
Anaphylaxis	6 (15.8%)	–	
Food allergy	5 (13.2%)	1 (3.2%)	
Atopic dermatitis	1 (2.6%)	4 (12.9%)	

TP0956 | Investigation of the proper use and re-prescription of adrenaline auto-injectors in Japanese beekeepers after a honeybee sting

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Background: Stings from the Hymenoptera family of insects, which includes bees, vespids, and ants, can result in anaphylactic shock and death. The treatment of choice for anaphylactic shock after a Hymenoptera sting is adrenaline, typically administered via an adrenaline auto-injector (AAI). We surveyed Japanese beekeepers to examine the proper use of AAIs after a honeybee sting and the re-prescription of the AAI.

Method: Members of the Japan Beekeeping Association, which is the largest beekeeping organization in Japan, were contacted by both e-mail and telephone by representative staff of all 47 Japanese prefectures. Thirty-two of the prefectures distributed allergist-developed questionnaires on paper to the potential participants; valid responses were received from 668 participants. All questionnaires were completed between June 2017 and May 2018. The questionnaire included the following items: AAI prescription, honeybee sting experienced after AAI prescription, systemic reaction (SR) experienced after a honeybee sting, AAI use after a honeybee sting, and AAI re-prescription.

Results: AAIs had been prescribed to only 38 (33 men and 5 women) of the 668 participants (5.7%) to prevent anaphylactic reactions to honeybee stings. Of the 38 beekeepers, 29 (76.3%) experienced a honeybee sting after AAI prescription. Of the 29 beekeepers, 15 (51.7%) experienced a subsequent SR and 9 (31.0%) used an AAI when stung; all of the beekeepers who used an AAI immediately visited a hospital. In addition, 20 of the 26 beekeepers (76.9%) who needed to be re-prescribed an AAI were given re-prescriptions. Of the 29 beekeepers who experienced a honeybee sting after AAI prescription, 15 (51.7%) developed an SR; 9 of these 15 (60.0%) were treated with an AAI. In addition, of the 14 beekeepers who developed no SRs to a honeybee sting, none (100%) were treated with an AAI.

Conclusion: This study found that most Japanese beekeepers were not properly prescribed an AAI for a honeybee sting. Furthermore, the proper use of AAIs and their re-prescription is not widespread. Our results suggest that Japanese beekeeping organizations should consider AAI prescriptions and that physicians and other health care workers need to better educate not only beekeepers, but also all people prescribed an AAI to improve adherence and to increase awareness of the risk posed by SRs.

TP0957 | A case of severe anaphylaxis after wasp sting which revealed systemic mastocytosis with B-chronic lymphocytic leukemia

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Case Report:

Background: The correlation between severe hymenoptera venom anaphylaxis (HVAn) and systemic mastocytosis has been thoroughly described in the international literature in recent years. Although a variant of mastocytosis is the systematic mastocytosis with an associated haematological neoplasm(SM-AHN) include myeloproliferative neoplasms, the lymphoproliferative neoplasms associated with mastocytosis are scarce.

Case report: We present a case of a 60-year-old man who reported 6 episodes of severe anaphylaxis with hypotension without skin rash or angioedema after wasp stings over the last 6 years (1 episode per year, having used adrenaline autoinjector in the last 3 episodes). Allergologic examination revealed positive skin and in vitro (serum specific IgE) testing for common wasp and paper wasp. Baseline serum tryptase (bsT) was within normal range.

Additional testing revealed lymphocytosis (17 K/μL) without evidence of infection or hepato-splenomegaly and negative CT scanning for lymphoma. He was haematologically assessed and peripheral blood immunophenotype showed B lymphocytes 63.7% with characteristic Igκ DIM CD19 + CD5 + CD23 + CD20 DIM CD43 BR CD79b-CD22 DIM CD200 + ROR1 DIM CD38-. Bone morrow biopsy confirmed above diagnosis of B-CLL and diagnosed systematic mastocytosis with an associated hematological neoplasm after having 3 out of 4 minor WHO criteria for systemic mastocytosis (> 25% spindle shape, expression of CD25, positive mutation in KITD816V). To this day, patient is periodically monitored every three months by a haematologist and has not received any specific treatment for B-CLL. He is receiving specific venom immunotherapy for common wasp and paper wasp, following a rush desensitization scheme, without any reaction.

Conclusion: This the first to our knowledge presentation of a patient with HVAn and SM-AHNMD associated with lymphoproliferative neoplasm who undergone venom immunotherapy. Bone marrow examination is crucial in cases of severe HVAn and abnormal common blood count, despite bsT levels.

TP0958 | Inaugural and fatal anaphylaxis to wasp venom

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Background: Hymenoptera venom anaphylaxis (HVA) is responsible for about 20% of all fatal anaphylaxis cases (200 subjects/year in Europe) of which 40% occur as inaugural systemic reactions. We represent a case of fatal anaphylaxis to wasp venom in a young man.

Method: A 35-year-old man with history of hypertension treated with valsartan since 15 days, but no history of allergy was stung by a hymenoptera on the shoulder and immediately developed a transient local erythema and chest pain followed by syncope with cardio-respiratory arrest and vomiting. He had accused fatigue with vomiting since several days. No Flow estimated at 4 minutes. On arrival of the emergency medical service, cardiac rhythm was asystolic, non shockable by the semiautomatic external defibrillator. Cardiac activity was obtained after 17 minutes of cardiac massage and 3 i.v. bolus of epinephrine 1 mg. In the Intensive Care Unit, the Coma Glasgow Score was 3/15 after 96 hours without sedation. The patient developed a post anoxic myoclonic status and brainstem reflexes disappeared. The EEG was unreactive, a bilateral absence of N20 waves of short-latency somatosensory evoked potentials was noted. The patient died 15 days later after terminal extubation.

Results: Serum tryptase 4 hours after the accident measured 1435 μg/L, whereas serum basal tryptase (sBT) levels on day 3 and 4 were found at 25.6 μg/L and 24.2 μg/L respectively, suggestive of an unknown indolent systemic mastocytosis (ISM). Specific IgE were positive for the 2 wasp venoms, but not for honeybee venom.

Conclusion: Risk factors for fatal HVA appear to be postural change, cardiovascular disease, mastocytosis, male sex, middle age and white race. The state of fatigue with vomiting might have contributed to the severity of the reaction as cofactor. Resuscitation maneuvers seem not to influence tryptase levels. SBT of 28 μg/L is found to be associated with a maximal risk of sting-induced anaphylaxis in ISM patients.

34% of ISM patients develop a systemic sting reaction of which 70% are very severe at the 1st systemic reaction. The recurrence rate in the absence of VIT is 97.5% in ISM patients.

This case of inaugural fatal HVA with unknown underlying ISM emphasizes the importance of sBT assessment even in case of a local reaction induced by a hymenoptera sting, as well as the importance, proposed by Vos et al., of hymenoptera venom specific IgE screening in all ISM patients and discussion of VIT on a preventive basis for some sensitized ISM patients (exposed subject).

TP0960 | Omalizumab as a premedication in venom immunotherapy: When is it indicated in systemic mastocytosis?

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Background: In systemic mastocytosis (SM) insect stings are one of the most important causes of anaphylaxis. Recent literature has reported the use of omalizumab as a premedication to decrease adverse effects occurred during venom immunotherapy (VIT) although consensus statement is needed.

Method: In this case series, we reported demographic and clinical characteristics of 9 patients with SM and the VIT schedules depending on whether premedication with omalizumab was applied or not.

Results: Four patients were female (44.4%) and the mean age was 49.6 ± 10.7 years. Bone marrow biopsies of all patients were compatible with SM. The median tryptase level was 25.8 μg/L (16-150) and C-Kit D816V mutation was positive in 8 patients. In the history, types of venom were bee, wasp and both in 5, 1 and 2 patients respectively and 1 patient was unaware of the insect type. All patients had grade 4 systemic reactions. Seven patients underwent VIT (4 for bee, 1 for wasp and 2 for both venoms) and two patients refused to receive VIT. Four patients received monthly 150 mg of omalizumab three months before VIT while in 3 patients VIT started without omalizumab. Among the patients who received omalizumab, one patient (Patient no:7) experienced anaphylaxis during skin prick tests and the other (Patient no:6) during the first dose of VIT and both had to receive adrenaline. Therefore, omalizumab was started afterwards. The other two patients were diagnosed as mastocytosis prior to VIT and therefore received omalizumab, whereas the other three patients were diagnosed as mastocytosis after the updosing period of VIT and did not receive omalizumab and had no reactions during VIT. Six patients received clustered and one patient had conventional VIT (Patient no:6). In one patient (Patient no:6) who was pretreated with omalizumab before VIT, grade 4 reaction occurred at the 6th week of VIT. In the 3rd year of treatment bee stung that patient and no problem occurred.

Conclusion: Omalizumab may be considered as a premedication in patients who experience reactions during skin tests and VIT but systemic reaction may develop in patients under omalizumab premedication and precaution should be considered during VIT.

n = 9 Patients	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9
Age	46	44	34	51	50	39	59	70	54
Gender	Male	Male	Male	Female	Female	Male	Female	Female	Male
Types of venom in history	Bee	Unknown	Bee	Bee	Wasp	Bee	Bee and Wasp	Bee	Bee and Wasp
Grade of reactions in history	Grade 4	Grade 4	Grade 4	Grade 4	Grade 4	Grade 4	Grade 4	Grade 4	Grade 4
VIT	Bee	Bee and Wasp	Refused by patient	Bee	Wasp	Bee	Bee and wasp	Bee	Refused by patient
Side effects during VIT	No reaction	No reaction	-	No reaction	No reaction	Systemic reaction	No reaction	No reaction	-
Prick tests	Bee +Wasp-	Bee +Wasp-	Bee -Wasp-	Bee +Wasp-	Bee -Wasp-	Bee +Wasp-	Bee +Wasp+	Bee +Wasp-	Bee -Wasp-
Total IgE kU/L	62.6	55	-	-	65	219	13.7	16	29.6
Specific IgEkU/L	Bee :0.27 Wasp:0.04	Bee :1.13 Wasp:1.35	Bee :0.75 Wasp:0.01	Bee :0.01 Wasp:0.01	Bee :0.05 Wasp:1.76	Bee :1.46 Wasp:0.39	Bee :0.001 Wasp:0.001	Bee :10.1 Wasp:1.1	Bee :3.6 Wasp:1.17
Tryptase µg/L	76.7	17.2	24	150	27	25.8	29.3	16	16.1
C-Kit D816V mutation	+	+	+	+	+	-	+	+	+
Omalizumab	-	-	-	+	-	+	+	+	-

TP0961 | Hymenoptera venom immunotherapy administration through a subcutaneous infusion pump: A safe and effective way to deliver immunotherapy in Chile

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Background: Systemic allergic reactions to Hymenoptera venom can be deadly. Intramuscular injection of adrenaline is used for an acute event. Long term specific immunotherapy (IT) for Hymenoptera venom can prevent a new systemic allergic reaction in 75-90% of the cases. There are different administration protocols for IT during the up-dosing phase: traditional (12 weeks), rush, ultra rush, and cluster, that shortens this starting period. Our objective is to describe and analyse the safety of a 4 week cluster, up-dosing phase protocol of Hymenoptera venom IT dispensed through a subcutaneous infusion pump (IP).

Method: Observational, descriptive, prospective, case report study, based on the review of clinical records of the starting sessions for Hymenoptera venom IT, using a cluster protocol dispensed by a subcutaneous IP, at the Allergy Unit, Clinica Alemana de Santiago, from January 2016 to December 2018.

Written informed consent was obtained from all patients.

Results: 19 patients, ranging from 4 to 62 years of age (average 17), 13 men, 14 lived in urban setting, 6 had history of atopy, 1 had hypertension. All had the diagnosis of Hymenoptera venom anaphylaxis, 15 were allergic to Apis mellifera and 4 to Vespula. In total, there were 76 doses dispensed by subcutaneous IP. 30 doses presented local reactions (39.4%): 17 immediate reactions, 13 delayed reactions. There were 5 grade 1 immediate systemic reactions (6.6%), all treated with antihistamines, with good clinical response. These systemic reactions were observed in 3 patients.

Conclusion: Subcutaneous administration of IT through a pump, is not free of neither local nor systemic allergic reactions. However, all of these were minor and responded well to regular treatment. Our findings are similar to other cluster protocols reported in the literature. In Chile, reducing the number of sessions is important as it improves adherence to treatment and quality of life of patients, reducing economic costs, without a significant increase of adverse reactions to IT.

Week	Vial	Dose (mL)	µg per dose	Administration
0	Maintenance	0.1	10 µg	IP
1	Maintenance	0.5	50 µg	IP
2	Maintenance	1	100 µg	IP
4	Maintenance	1	100 µg	IP
8	Maintenance	1	100 µg	Without IP

TP0962 | Field re-stings in patients receiving hymenoptera venom immunotherapy

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Background: Systemic allergic sting reactions are prevented by venom immunotherapy (VIT). However, there are few data about outcome of re-sting reactions occurring in the field. The aim of the study was to investigate the outcome of field re-stings in patients during or after completion of VIT and to identify patients at higher risk.

Method: A total of 115 patients (mean age: 38.5 ± 12 years, F/M: 45/70) treated with VIT between 1995-2018 years were included. They were called by telephone to invite for an interview in the clinic. A questionnaire about field sting and details of reaction history were filled out at this follow-up visit. The medical records of patients were screened from their files.

Results: Seventy four out of 115 patients (64.3%) were contacted to evaluate and asked about possible field stings during and after VIT. Thirty-eight patients had 70 times re-sting history in whom 25 were vaccinated with bee venom and 13 with vespula venom. Among them, 18 (25.7%) were systemic allergic reactions in which 8 (44%) reactions occurring with bee (1 grade 1, 6 grade 2, 1 grade 3) and 10 (56%) with vespula sting (1 grade 1, 5 grade 2, 4 grade 3). There was no difference in severity of index and re-sting reaction as well as bee or vespula venom sting. However, median duration of VIT was longer in patients showing no reaction than in patients with systemic reaction. Although seven patients have been using ACE inhibitor or beta-blocker drug, only 1 patient who was diagnosed as asthma and was on ACE inhibitor treatment developed two Grade 2 systemic allergic reaction due to re-sting during the first year of VIT.

Conclusion: This study indicates that VIT lasting for at least 3 years is more effective in protecting from systemic allergic reactions after field re-stings than shorter duration of VIT.

TP0963 | Presence of diabetes mellitus and history of drug allergy can increase the risk of ineffectiveness of venom immunotherapy

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Background: Venom immunotherapy (VIT) decreases the mortality and morbidity in venom hypersensitive patients. However, there are not enough data about the factors playing role in the ineffectiveness of VIT. The aim of the study was to investigate the features of patients that may have an effect on the severity of a field sting reaction during VIT.

Method: 121 patients who underwent VIT were included in the study. Demographic and clinical features were collected from their medical records and also from a questionnaire evaluating information about re-exposure to field stings. All these findings were compared between patients who have experienced systemic hypersensitivity reactions (HR)s after a field sting and those who have not.

Results: The mean age of the patients was 44.97 ± 13.93 years and 57.9% of them were male. Types of the venom extract used in immunotherapies were bee, wasp and both in 53, 25 and 41 patients respectively. The median duration of VIT was 16 months (min-max: 1-60 months). Four patients had systemic mastocytosis. Eight and 13 patients had atopy and history of a drug allergy. A 38.8% of the patients had comorbid diseases most commonly including hypertension (23.1%), coronary artery disease (13.2%) and diabetes mellitus (13.2%). 47 patients were using concomitant drugs mainly ACEI/ARBs (n = 21) and beta blockers (n = 21). The initial reaction was anaphylaxis in 84.3% (n = 102) of the patients and 31 patients experienced hypersensitivity reactions during VIT majority of which were milder than the initial reaction. 34 patients were re-exposed to a field sting and in 15 patients had field sting induced HRs, and 8 of them were systemic. When we compare the features of the patients who had or did not have a field sting induced systemic HR, we observed that female gender, diabetes mellitus and history of drug allergy were more common in patients with systemic HRs ($P = 0.031$; $P = 0.027$; $P = 0.027$). In multivariate analysis, presence of diabetes mellitus and history of drug allergy were associated with the field sting induced systemic HRs ($P = 0.041$; $P = 0.041$).

Conclusion: VIT is a highly protective treatment in venom induced systemic HRs. Presence of diabetes mellitus and history of drug allergy might be risk factors for ineffectiveness.

TP0964 | Efficacy and safety of venom immunotherapy in a patient with mastocyte activation syndrome—Case report

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Case report: *Hymenoptera*, mainly vespid and honeybee venom allergy is a frequent cause of anaphylactic reactions in the Central Europe. Although many risk factors have been identified to be associated with severe systemic reactions after *Hymenoptera* sting, increased baseline level of serum tryptase and systemic mastocytosis are of particular importance. Mast cell activation syndrome is

a condition with hyperresponsive mast cells leading to symptoms similar to anaphylactic reactions.

We present a case of 54-year-old patient with the history of three rapid generalised anaphylactic reactions following vespid sting including tachycardia, sweating, dyspnea, hypotension, paralysis and loss of consciousness within 2-5 minutes after sting. Laboratory examination revealed increased specific IgE antibodies against *Ves v1* and *Ves v5* allergen components while specific IgE antibodies against vespid allergen extract were negative. Increased baseline level of serum tryptase was detected repeatedly (60.6 ng/L). Dermatologic examination excluded skin mastocytosis. Mast cell activation syndrome was suspected to be the reason of tryptase elevation since other examinations did not confirm the diagnosis of organ mastocytosis. Due to the high risk of reoccurrence of severe anaphylactic reactions in the background of mast cell activation syndrome, subcutaneous venom allergen immunotherapy (VIT) with vespid venom was initiated. Despite quick systemic reactions after natural exposure, VIT was well tolerated by the patient. Laboratory tests during the VIT confirmed gradually increasing levels of protective IgG4 specific antibodies against vespid venom, transient increase of anti *Ves v5* antibodies and decrease of anti *Ves v1* antibodies. Three accidental expositions to vespid sting during the first year of allergen immunotherapy were not accompanied by any allergic reaction.

Serum tryptase level has to be analysed in all patients who underwent severe allergic reaction following *Hymenoptera* sting. Through this case report, we would like to point out importance of VIT in patients with the history of anaphylactic reaction to *Hymenoptera* sting and elevated baseline serum level of tryptase (with or without mastocytosis), as they are in extremely high risk of reoccurrence of severe life-threatening reactions.

TP0965 | Care of hymenoptera venom allergy: 12 years experience of a specialized department of algiers

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Background: The Hymenoptera venom allergy is an important cause of anaphylaxis. The prevalence of systemic reactions is 0.7 to 8% in the general population, from 0.34 to 8% in children, 14-32% among beekeepers. The risk populations are beekeepers and their families, pastry cook, people exercising outdoors. Prevalence is totally unknown and the treatment remains inadequate in our countries. The creation since December 2006 of a specialized center at the University Hospital Beni Messous (Algiers) for the diagnosis, treatment and prevention of Hymenoptera venom allergies. Risk factors are the severity of the initial reaction, age (adult), the type of insect (bee, wasp, hornet, bumblebee), the degree of exposure, the interval between injections and presence of cardio-respiratory diseases.

Method: This is a national prospective survey which took place from December 2006 to December 2018, on a sample of 506 patients (318 male and 188 female) with 100 children from 17 departments from Algeria. It took place at the hospital the day of the Pneumo -Allergologie Service (CHU Blessed Messous, Algiers). The average age of patients was 28 years, ranging from 06-62 years the examinations are conducted skin tests (bee and wasp) and IgE assay (bee and wasp).

Results: The concept of atopy was found in 46% of patients, 25% in those exercising exposed profession. We note a predominance of Stage III (43%) followed by Stages IV (32%) as classified by Muller, the tests are positive almost exclusively for bees, it is the same for specific IgE. From the 182 patients who were put under desensitization 32 are children, 179 are allergic to bee venom and 03 to wasp venom, 46 according to the rush protocol and 136 according to ultra-rush protocol with systematic health education for the sick ones.

Conclusion: Allergic reactions after Hymenoptera stings are potentially serious with a risk of death by anaphylactic shock. An emergency kit containing adrenaline must be prescribed to patients at risk. The desensitization has an efficiency superior to 90% to prevent the risk of second recurrence of a general reaction during later. There is a need for more specialized centers in the Maghreb and African countries to improve the diagnosis, treatment and prevention of allergies to Hymenoptera venom.

TP0966 | The role of component resolved diagnosis in hymenoptera venom allergy

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Background: Hymenoptera venom allergy is an IgE-mediated hypersensitivity reaction to Hymenoptera venoms. Occasionally, patients are not aware of the insect type that they have been exposed to and such uncertainties in history cause many problems related to diagnosis. In this study, the contribution of component resolved diagnostics (CRD) were evaluated in patients who had a systemic reaction due to a Hymenoptera.

Method: 81 patients from 5 different centers were included in the study. Prick, intradermal skin with venom extracts were performed and serum specific IgE levels for whole venoms were measured. sIgEs for Api m1, Api m2, Api m10, Ves v1, Ves v5 were evaluated

by venom allergen components by immunoblot method (Dpd-Dx Venom kit 2).

Results: Seventeen out of 33 patients with bee venom allergy revealed a positive skin test result and/or a high sIgE level to honeybee venom whereas 16 patients had positivity with both venoms. In 11 out of 17 patients with bee venom allergy, the diagnosis was confirmed with CRD whereas CRD was negative in the remaining 6 patients. In 13 of the bee allergic patients with double positivity to both venoms (13/16), double sensitivity was confirmed with CRD. CRD revealed a sensitivity of 73% in bee venom allergic patients. Seven of 18 patients with wasp venom allergy demonstrated sensitivity only to Vespula spp according to skin tests and/or sIgE levels whereas 11 patients revealed double positivity. Total sensitivity of Ves v1 and Ves v5 was calculated as 88%. Eight of 20 patients with a history of hypersensitivity to both venoms showed double sensitivity with CRD, one patient revealed cross-reactivity, seven patients was found sensitive only to bee venom, and finally one patient was sensitive only to Vespula spp. 10 patients were uncertain for the culprit insect type and half of them had double sensitivity and one had cross-reactivity according to CRD.

Conclusion: CRD seems to be more helpful in diagnosing wasp venom allergy than bee venom allergy. It also gives information to differentiate double sensitivity from cross-reactivity and in cases where the culprit insect is unknown.

TP0967 | Comparison of allergen sensitization profile in patients with honeybee venom allergy with immunoCAP and immunoblotting

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Background: In routine clinical practice, the profile of sensitization of patients is established by the specific allergens available in the ImmunoCAP system. This information can be very valuable to interpret the effectiveness of the treatment or possible adverse reactions caused by it. However, not all allergens described for *Apis mellifera* are available in this system. The aim of this study is analysed the *Apis mellifera* allergen sensitization profile in a group of patients diagnosed with honeybee venom allergy using immunoblotting with autochthonous venom and compare it with ImmunoCAP.

Method: The inclusion criteria of the allergy patients is who have been suffered a systemic reaction after a bee sting, with *Apis mellifera* venom allergy diagnostic and no previously treated with venom immunotherapy. The Immunodetection of specific IgE was done against total bee venom and bee venom allergens (ImmunoCAP).

Protein extract form autochthon venom was resolved in SDS-PAGE and transfer to PVDF membrane for the immunodetection using the patient's sera.

Results: Sera from 51 patients were analysed: 43 man, 8 women with a median age of 49 years (IQR 42 – 59 y). A 68.6% of the patients were beekeepers.

The main sensitization using ImmunoCAP were to rApi m 1 (Phospholipase A2) and rApi m 10 (Icaridin). A total of 90.2% and 74.5% of the patients respectively, were sensitized. The immunoblotting showed sIgE to nApi m 1 in 100%, nApi m 6 81.6% and nApi m 10 in 55.1% of the sera.

It is remarkable the low sensitization to Api m 2 (Hyaluronidase) and Api m 5 (Dipeptidyl peptidase 4) using immunoblotting, compared to ImmunoCAP.

Conclusion: All the patients were sensitized to Api m 1.

Api m 1, Api m 6 and Api m 10 are the major allergens in our patients. There is no correlation between ImmunoCAP and Immunoblotting techniques for allergens Api m 2, Api m 3 and Api m 5.

TP0968 | Determination of the presence of component-resolved diagnosis and other relevant allergens in honeybee venom through mass spectrometry

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Background: Allergy to hymenoptera venom (HVA) is one of the most common causes of anaphylactic reactions in allergic individuals that occur in response to stings of Hymenoptera such as honeybee or vespids. Diagnosis of hymenoptera venom allergy forms the basis of treatment which should be based on the use of well-defined, and properly characterized allergenic extracts according to allow identifying the causative agents to reduce the risk of future systemic reactions.

Method: The aim of this study was the identification and calculations relative abundances of the allergens present in a honeybee venom allergenic extract by mass spectrometry, following two different strategies. In gel-digestion approach, proteins separated on SDS-PAGE gel were digested. To increase in the depth characterization of venom extract, a direct in-solution trypsin digestion of proteins was done, and peptides were identified by LC-MS. This approach also allows us to estimate the relative abundances of the proteins identified by shotgun proteomics.

Results: In gel-digestion approach, bands resolved were identified. Api m 1 (30.00%), Api m 2 (1.37%), Api m 3 (0.17%), Api m 4 (35.34%), Api m 5 (1.47%), Api m 6 (3.87%), Api m 7 (2.41%), Api m 8 (0.23%)

Api m 9 (0.63%), Api m 10 (1.26%) and Api m 11 (1.50%) were identified in solution digestion approach, in venom extract.

Conclusion: The combination of both strategies allows us to identify the component-resolved diagnosis and other relevant allergens in honeybee venom extract, reported by IUIS data base. The production process of therapeutic allergenic extracts must be standardized. The information that provides the use of mass spectrometry techniques about the presence of clinically relevant allergens facilitates the use of highly reliable Hymenoptera allergenic extracts.

TP0969 | The role molecular diagnostic in hymenoptera venom allergic Serbian patients

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Background: Detection of serum-specific immunoglobulin E (sIgE) to specific and cross-reactive venom allergens facilitate the discrimination between primary sensitization and cross-reactivity and to provide a better selection of venoms for venom immunotherapy (VIT), particularly in patients sensitized to both honeybee (HBV) and wasp venom (WV). Component-resolved analysis with recombinant species-specific major allergens (rSSMA) may help to distinguish true sensitization from crossreactivity.

Method: We analyzed 66 patients with hymenoptera venom allergy (HVA), 42 with double positivity of sIgE to both whole venoms and 24 with single positivity to HBV or WV whole venoms. We determined the frequency, sensitivity and specificity of sIgE to rApi m 1 honeybee and rVes v 5 wasp venoms, and grade of the systemic allergy reaction (SAR) according to Mueller in patients with HVA. In allergic patient's sIgE to rApi m 1, rVes v 5 and cross-reactive carbohydrate determinants (CCDs) were tested by ImmunoCAP.

Results: We detected sIgE to rApi m 1 in 10 (24%) and sIgE to rVes v 5 in 18 (43%) allergic patients. Three out of 42 patients was double negative. Only 26% of 42 with double positivity to whole venoms reacted to rSSMA of both species. Frequency of sIgE to CCDs was 40%. Sensitivity of sIgE to rVes v 5 (100%) and specificity of sIgE to rApi m 1 (100%) and rVes v 5 (93%) was very high, but sensitivity to sIgE to rApi m 1 was 71%. Severe SAR in our 66 patients was very high (>85%).

Conclusion: Specificity of sIgE to rApi m 1 and rVes v 5 and sensitivity of sIgE to rVes v 5 is very high. Sensitivity of sIgE to rApi m 1 could be increased by adding rSSMA of other bee venom allergens. Recombinant allergens improve the diagnosis and treatment of Hymenoptera venom allergy.

SUNDAY, 2 JUNE 2019
TPS 20
ANAPHYLAXIS, MASTOCYTOSIS AND CUTANEOUS ALLERGIC REACTIONS

TP0970 | Post-mortem tryptase cut-off points of main causes of fatal anaphylaxis

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Background: Few studies have studied the best cut-off point for post-mortem tryptase in fatal anaphylaxis, resulting a very wide range of values (10-110 μg/L) and small number of cases for all studies. In this study we report for post-mortem tryptase cut-off point in a series of 37 deaths due to anaphylaxis.

Method: 122 cases of deaths, with the suspicion of anaphylaxis as cause of deaths were assessed by 2 allergists, with the proposal to confirm the diagnosis of anaphylaxis. The cases were provided by the National Institute of Forensic Sciences and Toxicology. We decided to use ROC curves, in order to find the best post-mortem tryptase cut-off points that classify all causes of anaphylaxis and each cause of anaphylaxis (drugs, hymenoptera stings, and food), using as gold-standard the diagnosis of anaphylaxis made by two allergists.

Results: According to the criteria used by 2 expert allergists, 46 cases submitted to the INTCF were diagnosed as anaphylaxis, although 39 anaphylactic deaths and 44 non-anaphylactic deaths had available tryptase determinations. The best cut-off point post-mortem tryptase to confirm anaphylaxis as the cause of death was 64 μg/L overall, 81.7 μg/L for drug anaphylaxis, 64 μg/L for anaphylaxis due to hymenoptera sting, and 54.4 μg/L for anaphylaxis due to foods. All cut- off points results were significant except for fatal anaphylaxis due to foods.

Conclusion: To our knowledge, we report the largest series which reported the best cut-off point tryptase for fatal anaphylaxis, which better accuracy than other published series. Future studies on the same topic, should include individual results for different causes of anaphylaxis, different times of sample extraction, and a higher number of cases.

TP0971 | Ultrasonography for diagnosing acute laryngeal edema in outpatient setting

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Background: There is an increased incidence of cases presenting in outpatient setting with acute laryngeal edema due to allergic reaction. This situation represents a medical emergency with a life threatening potential. Given the wide availability of ultrasound machines we analyzed the possibility of visualizing the glottis space by non ENT non radiology specialists.

Method: We propose a three steps technique of examining glottis space using a portable ultrasound machine equipped with a 12 MHz linear probe. First step is visualizing longitudinally on the neck midline the anatomy structures neighboring the hyoid bone. Second step is visualizing the pre epiglottis space with the enlargement of the epiglottis. Third step is visualizing transversely the thyroid cartilage with the enlarged vocal cords due to edema.

Results: We compared the images obtained by ENT specialist through nasal-pharyngo-laryngeal endoscopy in 10 consecutive cases with acute allergic laryngeal edema and the images obtained through the above mentioned three steps technique using sonography.

Conclusion: There is a strong correlation between the two methods for visualizing laryngeal edema. Moreover ultrasound is fast, lacks irradiation and with minimal training the specialists in outpatient clinics could visualize laryngeal edema and thus expedite the treatment.

TP0972 | Non food related exercise induced anaphylaxis in a 11 years old male

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Case report: Introduction: Exercise-induced anaphylaxis (EIA) is not a common health condition and consists in a disorder in which anaphylaxis occurs in response to physical exertion. There are only low-quality evidence and clinical experience on which to base individualized management for each patient.

Case: We are presenting the case of one 11 years old male with history of urticaria in lower extremities since the age of 6 months

occurring after episodes of prolonged crying, which persisted during the growth. The patient has been examined continuously and received normal ranges of total IgE, negative results of patch tests, skin prick tests for pneuma and tropho allergens.

In March 2018, during physical education, after exercises had generalised urticaria accompanied with dyspnea and has been transferred and treated in emergency department. Two months later the patient has been presented at Allergology Clinic where the effort test was done. On the fifth minute of the examination the patient showed widespread flushing of the skin, swelling of the face, lips, ears and arms, abdominal pain, swollen tongue. Difficult and noisy breathing, wheezing, persistent cough with no pulmonary sounds. The examination test has been interrupted and the patient has been treated immediately with loratadine 10 mg po and parenteral prednisolone 50 mg IV, saline solution. After 1 hour the clinical situation has been improved, but urticaria still persistent. After the examination the diagnosis of Exercise induced anaphylaxis was confirmed and the patient has been treated for 2 months with desloratadine 5 mg, 1 tablets per day and montelukast 5 mg 1 × 1 tablet per day. Actually the patient tolerates moderated physical efforts without any symptoms.

Conclusion: This case presents a successful dominated exercise induced anaphylaxis with oral antihistamines and antileukotrienes in a male teenager with childhood history of EIA.

TP0974 | Pathologic characteristics of fatal anaphylaxis: A Spanish nationwide 17- year series

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Background: Forensic series and data from clinical-administrative cohorts on fatal anaphylaxis are scarce, probably because diagnosis of sudden death is often complex and also because its incidence is very low. We report on the histopathologic characteristics of a series of sudden deaths which were investigated for anaphylaxis at the Spanish National Institute of Toxicology and Forensic Sciences (INTCF) over a 17-year period.

Method: A total of 122 undetermined sudden deaths sent for assessment to the Provincial Institutes of Legal Medicine and Forensic Sciences (INTCF), from different regions of Spain, with anaphylaxis as the suspected cause of death, underwent histological, biochemical, and clinical investigation during the years 1998-2015. Research based on several analyses was carried out according to the protocol included in the rules for sending samples to the INTCF (Official Spanish State Gazette, Ministry of Justice, BOE order JUS/1291/2010), including biological, toxicological, and histopathological studies.

Results: Two certified allergists confirmed that 46 of the 122 cases were classified as fatal anaphylaxis. Histopathology data were available for 40 (86.96%) individuals. The most frequent autopsy findings were angioedema of the upper airways (43.48%), pulmonary edema (41.30%), atheromatosis of coronary vessels (28.26%) and of non coronary vessels (30.43%), and pulmonary congestion (24%). In our series, microscopic and macroscopic findings were not found in only 7 cases (15.22% of 46 patients with anaphylaxis).

Conclusion: Our findings for fatal anaphylaxis indicated the most frequent manifestations were pulmonary and upper airway edema followed by coronary atherosclerosis. The post-mortem findings for fatal anaphylaxis are nonspecific and vary considerably, according to published in the literature. Our figures were similar to the reported intermediate values, and as described also in the international literature, our findings were not specific.

TP0975 | Severe and refractory anaphylaxis due to rupture of hydatid liver cyst

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Case report: Background: Hydatid cyst is a serious parasitic infection in places which people has a close contact with dogs or sheep and is primarily caused by the larvae of Echinococcus granulosus. Hydatid cysts may be complicated if rupture of the cysts occurs due to blunt trauma or spontaneous increases of intra-cystic pressure. Spontaneous or traumatic rupture of cyst and the presence of antigenic content into the systemic circulation may result in allergic reactions such as urticaria, angioneurotic edema, asthma and anaphylaxis. Here, we reported a case of severe and refractory anaphylaxis due to rupture of hydatid liver cyst which was previously unrecognized.

Case report: Fifteen-year-old female was admitted to the emergency department of our hospital with symptoms of syncope, generalized flushing, abdominal pain occurring while kick box training. She had generalized flushing. Her arterial blood pressure was 75/45, pulse was 110/min at admission. She was diagnosed with anaphylaxis and was brought to the trendelenburg position and intramuscular adrenaline was administered. She received isotonic saline infusion in 15 min. Ranitidine, methylprednisolone and pheniramine were administered intravenously. Because of hypotension, flushing and abdominal pain continued inspite of therapy, another dose of intramuscular adrenaline was administered twice with 5 min intervals. In total 40 cc/kg isotonic saline was administered.

Adrenaline infusion was started due to refractory hypotension absence of any improvement of clinical findings. Clinical findings improved on 8th hour of the infusion and adrenaline infusion was discontinued. Generalized flushing, angioedema and hypotension were developed one hour after discontinuation of adrenaline infusion. Intramuscular adrenaline was administered again and then adrenaline infusion was started. History has deepened and it was learnt that the abdomen was hit during kick box training. Abdominal USG was performed and the diagnosis of rupture of hydatid liver cyst was confirmed.

Conclusion: Anaphylaxis is a life-threatening condition. Regardless of etiology, any cases of anaphylaxis should be treated appropriately. In patients with anaphylaxis presenting to the emergency department, if the etiologic agent cannot be detected, if there is a fluctuating course in the clinic like our patient, hydatid rupture should be considered even if there is no history of trauma.

TP0977 | Case report: Human seminal plasma allergy (HSPA) and dog epithelium allergy in Brazil

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Case report: Introduction: HSPA is a rare phenomenon, typically under recognized, that affects young female adults. Its clinical manifestations range from local reactions (vulvar/vaginal itching and erythema) to life-threatening anaphylaxis during or after sexual intercourse. It is most likely mediated by a classical IgE mechanism, and PSA is thought to be a causative allergen. It has been recently reported that a prostatic kallikrein protein isolated from dog dander extract can cross-react with human PSA, which suggests that dog epithelium allergy might be a risk factor for HSPA.

Case Report: A 22- year-old woman, dog-owner, goes to our private clinic to treat symptoms of allergic rhinitis. The clinical history showed that after one year of relationship with her boyfriend she started presenting mild eyelid angioedema 30 minutes after sexual intercourse. This symptom got gradually worse over time, until one day she presented running nose, dyspnea and bronchospasm, which led her to an emergency care. She had other partners and never had these reactions before. She has family history of atopy, never used intrauterine device or had any gynecological procedure. Her total serum IgE (ImmunoCAP®), specific IgE to dust mite and dog dander were elevated, while her specific IgE to latex was negative. The use of condom during the sexual intercourse was oriented and the patient never presented symptoms again. After 4 years (2018), she returned to our clinic complaining she once experienced mild eyelid angioedema and running nose, after coitus interruptus. She also expressed her desire to get pregnant. A skin prick test was performed with her partner seminal fluid and specific IgE to seminal fluid was collected. Both tests were positive.

Conclusion: HSPA is a rare clinical condition, with several differential diagnosis, and few described cases in peer-reviewed literature. Clinical history, especially linked to sexual intercourse, and *in vivo* and *in vitro* tests are necessary for diagnosis. In developing countries, the limited access to the required tests presents a challenge to the diagnosis. Thus, this explains, to some extent, the few developing countries case reports available in the literature. This case report presents a HSPA in Brazil, which exhibits the relationship between dog epithelium allergy and HSPA. The patient received the diagnosis with relief, since the symptoms were depreciated by previous physicians.

TP0978 | Conut score as a tool for early detection of poor nutritional status in advances forms of SM

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Background: Mastocytosis is a disease of the bone marrow caused by the proliferation of the mast cells. The clinical course of mastocytosis may differ from cutaneous, indolent to aggressive forms. Malnutrition and weight loss are important symptoms in many patients. The aim of the study was to assess the nutritional status using CONUT score in clinical forms of mastocytosis.

Method: Controlling Nutritional Status (CONUT) score, calculated based on the serum Alb concentration, total peripheral lymphocyte count and total cholesterol (TC) concentration was used in

109 mastocytosis patients gathered in the European Competence Network on Mastocytosis database.

Results: Poor nutritional status CONUT SCORE ≥ 3 more often in advances forms of SM $P = 0.00001$. Proper nutritional status CONUT SCORE < 2 more often in ISM, SSM, MPCM and DCM $P = 0.003$

Conclusion: CONUT SCORE is useful tool for early detection of poor nutritional status especially in advances forms of SM (ASM, SM-AHN).

DIAGNOSIS	CONUT 0-1	CONUT 2-4	CONUT 5-8	CONUT 9-12	TOTAL
ISM	52	15	1		68
MPCM	11	4	0		15
MIS	5	4			9
ASM	1	2	1	1	5
DCM	1				1
SM-AHN	2	2	2		6
SSM		4	1		5

TP0979 | Do pharmacists know how to use adrenaline autoinjectors?

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Background: Adrenaline autoinjectors (AAI) are the most effective treatment of anaphylaxis in community settings. Adrenaline is potentially lifesaving if the patient is capable of injecting it early and correctly. Community pharmacists supply these devices and they have an important role in teaching patients how to use them.

Aim: To assess whether pharmacy workers, pharmacists and pharmacy technicians (PW) were able to correctly demonstrate and teach the use of an AAI.

Method: A survey was carried out in pharmacies in the cities of Porto and Chaves between May 2018 and December 2018. The pharmacists were invited to simulate adrenaline administration with trainers of the 2 currently available AAIs (Epipen® and Anapen®).

Results: A total of 31 questionnaires were included; 24 (77%) female, 19 (61%) pharmacists, median age 40 years. Of the total, 29 (94%) knew the name of at least one of the AAI and 20 (65%) knew both. Twenty-nine (94%) stated that they had no previous training or information on how to use an AAI; 26 (84%) had sold at least one AAI. None of the PW had ever been questioned by patients on how to use AAI and, although none was ever asked by a patient how he should use it, and 22 (71%) had no idea which AAI would be easier to use or to teach.

Concerning the use of the trainers, 9 (29%) were not able to commence the process with Anapen® and 2 (7%) with Epipen®; 17 (55%) would be able to inject themselves with adrenaline with both AAIs but failed the last step "massage injection site". Only 3 (10%) managed to accurately simulate the Anapen® trainer and 4 (13%) the Epipen®. After demonstrating the proper use of both AAIs, 23 (74%) of the PW considered Epipen® easier to use and easier to teach.

Conclusion: Almost half of the pharmacists were unable to correctly inject adrenaline with the trainers. So there is room for improvement since adrenaline auto-injector prescriptions are on the rise and community pharmacies could have a crucial role in teaching patients on their use.

TP0980 | Histopathological criteria for mastocytosis in the skin

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Background: The diagnosis of mastocytosis in the skin (MIS) can be challenging. To confirm or exclude a suspicion of MIS skin biopsies are often needed. Histological criteria for bone marrow mastocytosis include mast cell aggregates, spindle-shaped mast cells and staining with CD25 or CD2. For MIS, however, no clear histopathological criteria are defined.

Method: We performed immunohistochemical staining for tryptase, CD2, CD3, CD25 and CD117 on formalin-fixed paraffin-embedded skin of 26 cases of typical dermatologist-confirmed MIS and 36 control cases (urticaria, eczema, pruritus sine materia, excess skin from dermatologic surgery). The quantity of mast cells and T cells per mm² was counted in the upper 900 µm of the skin; for mast cells by separately counting three consecutive layers of 300 µm. In addition, the size of ten representative mast cells per case were measured and the cell morphology was categorized as "spindle-shaped" or "not spindle-shaped".

Results: CD117 and tryptase staining showed comparable results with median mast cell density in MIS biopsies of 134 cells/mm², both. Control cases showed significantly lower median mast cell densities ($P < 0.001$) between 27 (urticaria) and 37 (eczema) cells/mm². In MIS, mast cells were predominantly located in the superficial subepidermal skin layer (median = 247 cells/mm²) and there was a characteristic significant decrease ($P < 0.0001$) of mast cell density towards the deeper layers (80 cells/mm² for 300-600 µm and 35 cells/mm² for 600-900 µm). This gradient was not significant in the control group ($P = 0.288$). A mast cell density cutoff of 62 cells/mm² in the subepidermal layer of the dermis had a sensitivity as well as specificity of 92% for MIS (CD117). We found no difference concerning mast cell morphology or mast cell size. CD2 staining for mast cells was negative in all cases, whereas CD25 staining was positive in one case of MIS. Unexpectedly, T cells were present within the infiltrate not only in inflammatory control skin, but also in 77% of MIS tissues.

Conclusion: In contrast to bone marrow mastocytosis, CD2 and CD25 staining as well as morphology were not relevant for the histological diagnosis of MIS. T cells infiltrates were not specific for

inflammatory differential diagnoses. Increased mast cell numbers located predominantly in the uppermost levels of the dermis is the main histopathological criterium for the diagnosis of MIS.

TP0981 | Impact of allergic disorders and anaphylaxis in mastocytosis, based on the ECNM database

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Background: Mastocytosis is a neoplastic disease caused by abnormal proliferation of mast cells related with an increased risk of anaphylaxis. European Competence network on mastocytosis initiated a database focused on prevalence, prognosis, the evolution of various forms of the disease. The current study is focused on symptoms of allergy and anaphylaxis

Method: The data on 2386 patients were studied, among them 816 presenting symptoms of anaphylaxis.

Results: Insect venom allergy (IVA) was diagnosed in 16.5%, food allergy in 4.2%, drug allergy in 5% of subjects. The prevalence of IVA was highest in ISM patients (25.5%) compared with 4.8% in other forms of the disease ($P < 0.00001$), food allergy in DCM (11.5%), drug allergy in MCL (17.2%). Among IVA patients wasp allergy was the most prevalent (11.4%), bee allergy (2%) Polistes (1%), other patients presented multiple allergies. NSAIDS intolerance was found in 2% of subjects, antibiotic allergy in 2%, all other drugs 1%. Patients with allergy presented lower % of MC infiltrates in IHC (12.8 vs 20.3% $P < 0.00001$) lower tryptase (56/9 vs 76.1 ng/mL $P < 0.01$). Tryptase level in a range (10-70 ng/mL, mast cells in IHC ≤ 5% and ISM were related with an increased risk of allergy (OR = 1.87 CI 1.4-2.5) and IVA (OR = 3.8 CI2.7-5.3).

Conclusion: Insect venom allergy is more prevalent in mastocytosis compared to the general population (17% vs 2.5%). Wasp allergy (yellow jacket) is the most prevalent in IVA. NSAIDS (2%) and antibiotics (2%) intolerance is the most important drug allergy. Patients with ISM are the most susceptible to IVA, while patients with aggressive forms of mastocytosis suffer from drug intolerance Allergy score = ISM, tryptase (10-70) and (mast cells in IHC ≤ 5) is related to the increased risk of allergy OR = 1.87 and IVA OR = 3.8.

MONDAY, 3 JUNE 2019
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ATOPIC DERMATITIS AND MISCELLANEOUS

TP0983 | Therapeutic advantage of bacterially delivered toll-like receptor 8 MiRNA in atopic dermatitis

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Background: Atopic dermatitis (AD) is one of the most common chronic inflammatory skin diseases in children. Skin inflammation is caused by complex interactions between genetic disposition and aberrant innate/adaptive immune responses. Toll-like receptors (TLRs) are key molecules in innate/adaptive immune response by recognizing various molecular motifs associated with pathogens. Among them, TLR8 is implicated in eczematous skin reactions. We investigated the therapeutic effects of TLR8 suppression using miRNA on the modulation of inflammatory response.

Method: We used *Salmonella* as a vector to deliver *TLR8* miRNA. The recombinant strain of *Salmonella typhimurium* (ST) expressing *TLR8* miRNA (ST-miR*TLR8*) was prepared for knockdown of TLR8. After oral administration of ST-miR*TLR8* into mice, we observed cytokine levels, skin pathology and scratching behaviors in an AD-like mouse model.

Results: TLR8 down-regulation decreased macrophage-derived chemokine concentrations in activated human mast cells. Th2 cytokine levels were significantly decreased after oral administration of ST-miR*TLR8*. Serum IgE and interleukin-4 production were suppressed whereas IFN-γ was induced after treatment. Scratching behaviors and skin inflammation were also improved. In addition, attenuated *S. typhimurium* safely accumulated in mouse macrophages and showed adjuvant effects.

Conclusion: This study shows the recombinant miRNA which express the *TLR8* gene has therapeutic effects by suppressing Th2 inflammation. *TLR* gene modulation using miRNA via *Salmonella* vectors would have a double protective effect in the treatment of AD.

TP0984 | Dupilumab as treatment for severe recalcitrant atopic dermatitis - real life experience in an Austrian cohort

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Background: Atopic dermatitis (AD) is a chronic, relapsing skin disease characterized by intense pruritus, impaired skin barrier functions and increased susceptibility to cutaneous infections. Interleukin (IL)-4 and IL-13 are key cytokines of the Th2 immune response playing a crucial role in the pathogenesis of AD. Dupilumab, a fully human monoclonal antibody against IL-4Ralpha, targeting the shared subunit of IL-4 and IL-13, was recently approved for the treatment of moderate-to-severe atopic dermatitis in adults.

Method: In this retrospective observational study we aimed to assess the efficacy of dupilumab in patients with moderate to severe AD under real-life conditions. Data on the intensity of AD as measured by Eczema Area and Severity Index (EASI), Investigator Global Assessment (IGA) as well as by patient-oriented scores (Dermatology Quality of Life Index (DLQI), Numerical Rating Scale itch (NRS)) were evaluated in the course of dupilumab treatment. In addition, routine laboratory results as well as adverse events were analyzed.

Results: Patients had an IGA of 3 or 4 and a mean EASI score of 36 before treatment initiation. Already 6 weeks after starting dupilumab, 54% of patients had an IGA score of 0 to 1. They showed a mean EASI reduction of 58%, a mean itch reduction of 45% and 51% mean improvement of DLQI. Interestingly, the mean levels of eosinophilic cationic protein were lowered by 63% at week 6, whereas the levels of lactate dehydrogenase remained unchanged. Adverse events were mild with herpes simplex infections and conjunctivitis reported most frequently.

Conclusion: Under real-life conditions, dupilumab is an effective treatment of moderate-to-severe AD with a favorable safety profile.

TP0985 | Safety and efficacy of cyclosporine a in the treatment of severe atopic eczema in children and adolescents (experience of one centre)

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Background: Severe forms of atopic eczema (AE) represent a therapeutic challenge in both children and adults. Many topical and systemic therapies have been studied in management of AE with various successes. Cyclosporin A (CycA) is a potent immunosuppressant, calcineurin inhibitor, that inhibits cell-mediated immunity, mainly via inhibition of transcription of cytokine genes in activated T helper cells, NF-κB system and other signalling pathways (i.e. JNK, p38). It has been used successfully in the treatment of severe AE in children and adults. The aim of our work was to determine the

clinical profile of our paediatric patients with severe AE treated with CycA and their response to this therapy. We also evaluated the safety profile of CycA.

Method: We analysed 16 patients (3 females, 13 males) from our centre with severe AE that failed the conventional treatment and started therapy with CycA. All the subjects underwent regular clinical controls during one year connected with laboratory sampling.

Results: Altogether, 16 patients were included in our clinical observation. The age range from 5 to 20 (average 10.7) years. Positive family history for atopy in first-degree relatives had 11 patients. Age of the first skin symptoms range from 3 months to 3 years (average 1.5 year). Recurrent infections had 7 patients. Comorbidities were found in 13 patients, mainly ENT conditions or allergic conditions. Most patients had mild T-cell deficiency, others had mild to moderate natural killers deficiency, selective IgA deficiency or mannose-binding lectin deficiency. Serum concentration of IgE before therapy range from 72 IU/mL to more than 10 000 IU/mL. The average age of start of treatment with CycA was 9 years. The initiating dose of CycA was 3 mg/kg/day divided into 2 doses. Rapid improvement was seen within the first 2 weeks. The benefit was attained during the whole treatment. One patient experienced mild hair loss, other patient had hypertrichosis during the treatment. Serious adverse events or worsening of the deficiency in immune profile were not seen during treatment. The longest treatment time is 5 years.

Conclusion: Long-term and low-dose treatment with CycA is effective and safe in paediatric patients with severe AE refractory to conventional therapy. The potential for adverse events necessitates regular monitoring during its use. Nowadays, new treatment options are available for severe refractory AE, but mostly for adult patients. More clinical trials are needed, especially for paediatric patients.

TP0986 | Predicting skin barrier dysfunction and atopic dermatitis in early infancy

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Background: Dry skin, a cardinal sign of atopic dermatitis (AD), is associated with increased transepidermal water loss (TEWL), which is found to precede development of AD. The aim of this study was to identify predictive factors of dry skin, high TEWL, and AD at 3 months of age.

Method: From the randomized controlled birth cohort Preventing Atopic Dermatitis and Allergies in children (PreventADALL) trial enrolling mother-child pairs at 18-week pregnancy, we included all 1150 control infants who attended the 3-month follow-up visit. Infants were born with gestational age (GA) of at least 35.0 weeks. Clinical investigations at 3 months of age included skin examination and TEWL measurements. Socio-demographic data, parental disease and pregnancy related factors were recorded in electronic questionnaires at 18 and 34 weeks GA, and mode of delivery from birth charts. Eczema was used as a proxy for AD, and defined as the presence of eczematous lesions observed by study personnel, excluding differential diagnosis to AD. To identify predictors of dry skin, high TEWL (> 90th percentile/ > 11.3 g/m^2/h) or eczema at three months, we used a multivariate regression analysis with backward variable selection, including variables of $P < 0.2$, which were identified using univariate logistic regression analysis of 42 preselected parental and pregnancy- related variables.

Results: Predictive factors for dry skin were GA > 38 weeks (OR: 2.57, CI 95%: 1.74-3.82) and advanced paternal age, especially > 37 years (OR: 2.18, CI 95%: 1.47-3.23). Predictive factors for high TEWL was maternal allergic disease (OR: 2.03, CI 95%: 1.28-3.21), and birth during winter season (OR: 2.02, CI 95%: 1.31-3.10), while female gender was protective (OR: 0.60, CI 95%: 0.40-0.91). Predictive factors for eczema were elective caesarean section (OR: 2.23, CI 95%: 1.08-4.60), multiparity (OR: 1.97, CI 95%: 1.29-3.01), maternal allergic disease (OR: 1.78, CI 95%: 1.10-2.87), and paternal allergic disease (OR: 1.59, CI 95%: 1.05-2.42).

Conclusion: Distinct parental and pregnancy- related factors were predictive of infant dry skin, high TEWL and AD at three months of age.

TP0987 | Epidemiological study of atopic dermatitis in Mexico

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Background: Atopic dermatitis (AD) is a chronic inflammatory disease of the skin, triggered by the interaction of environmental and immunological factors. Its prevalence has increased in the last 30 years. There is little epidemiological information on its diagnosis and treatment in Mexico; it is important to know the criteria used for the diagnosis and treatment of AD by the different medical specialists in Mexico.

Method: with the authorization of the ethics committee, an electronic survey designed by the authors was applied to specialist doctors from different public health institutions in Mexico.

Results: We conducted 114 surveys, 56% of the participants were allergists, 38% dermatologists and 5% pediatricians of second and third level of medical care. 62% of the population they serve corresponds to > 18 years of age. The most used diagnostic criteria are the Hanifin and Rajka in 54%. Participating physicians request

laboratory tests such as total and/or specific IgE in 38%, prick test 19% and skin biopsy 6%. SCORAD is the severity scale used in 96% of doctors

Regarding age and severity, participants indicated that in < 18 years, mild DA corresponds to 90%, moderate 8% and severe 2% and in > 18 years: mild DA 89%, moderate DA 6% and severe DA 5%. 45% of participating physicians refer to prescribe the joint use of antihistamines, emollients, topical steroids and calcineurin inhibitors, another 36% add an additional drug such as cyclosporine, to achieve control of the disease.

Conclusion: Diseases' knowledge will allow the use of diagnostic criteria and scales of appropriate severity that favor correct prescriptions of medicines to obtain the control of the DA.

TP0988 | Prevalence and primary incidence of atopic dermatitis in armenia

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Background: The purpose of the work is to clarify the severity of the problem, its relevance to the main population of Armenia, to identify the risk factors.

Method: For the first time in Armenia the calculation of AtD morbidity and prevalence indicators was performed, including the process dynamics according to the age groups. An epidemiological study has been conducted based upon the reporting forms' data by the National Institute of Healthcare the Ministry of Health of the Republic of Armenia regarding the number of Atopic Dermatitis diagnosed cases for the period of 2008-2016.

Results: During 9 years the indicator in the group of "0-14 years old" has increased for 2.65 times: from 2.74 to 7.25. The growth rate made 165%. The primary incidence rate in the group of "15 years old and above" has reached 3.16 from the initial 1.47 and eventually increased for 2.15 times as compared to the initial level of 2008. The growth rate made 115%. And in total, throughout Armenia, the incidence rate rose from 1.71 to 3.96, which is 2.32 times more than the initial level. The growth rate made 132%. The same pattern is observed for the indicator of the AtD prevalence. In the group of "0-14 years old" the indicator increased for 2.57 times: from 3.62 to 9.31. The growth rate made 157%. In the group of "15 years old and above" it has increased twice: from 2.14 to 4.27, hence the growth rate made 100%; so in general, the AtD prevalence rate has increased for 2.17 times from its initial level of 2.42 up to 5.26, while the growth rate made 117%. The picture differs when considered by the regions. The rise of primary morbidity is truly striking, especially in the elder group. Based on the results, the findings show that the rates of AtD morbidity and prevalence rapidly grow, in some of the regions the number of patients per 1000 of population exceeds the number reflected in the literature. The largest indices were registered in the most forested and mountainous regions, where different climatic zones are found in one location. It should be noted that although AtD is considered a childhood illness, an increase in morbidity and prevalence rates is observed in all age groups.

Conclusion: This directs to a conclusion that the environmental factors can be quite effective in the AtD development.

TP0989 | Impact on the quality of life of patients with atopic dermatitis in different cities of Argentina

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Background: Atopic dermatitis is a chronic inflammatory skin disease, characterized by cutaneous dryness, pruritus and recurrent, bilateral and symmetrical outbreaks of eczema. The outbreaks favor a loss in the quality of sleep and rest, causing lower levels of personal performance in school, work and social environments, in addition to significant emotional affectation associated with the severity of the symptoms. The objective is evaluate the quality of life of patients with AD during maintenance treatment in our environment and compliance with the treatment for the control of the DA.

Method: We carried out an epidemiological, observational, multicenter, retrospective and cross-sectional study in pediatric and adult patients diagnosed with AD. We Applied to the study group the Dermatology Life Quality Index (DLQI), the Children's Dermatology Life Quality Index Questionnaire (CDLQI), the version for children under 4 years old (IDQOL) and the Morisky-Green test.

Results: Forty-one patients were included: 46% under 5 years old, 24% between 5 and 16 years old and 29% older than 17.

As a result, we found out that the quality of life was extremely affected in 9.76% of the cases, severely affected in 29.27%, moderately affected in 34.15%, and only a minority (4.88%) did not have their quality of life affected.

Children under 5 years old had, predominantly, been affected in the quality of life either in a severe way or in a small way, unlike the age groups over 6 years old, where their quality of life was moderately affected.

When evaluating treatment adherence, 76% is noncompliant. Of those who adhered to the treatment (24%), a 75% has dad a great impact on their quality of life (p: 0.05).

Conclusion: In the studied population the quality of life of the majority was affected from a moderate to a great manner and that 9.76%

was extremely affected. 76% of the population was considered non-compliant with the treatment and that of those who did, 3 out of 4 were extremely affected, it is inferred that when AD is more severe, patients are more likely to have a greater adherence to the treatments, so strategies should be planned to improve adherence in those patients with moderate symptoms, which represent more than 34% of the total.

TP0990 | Atopic dermatitis and impact on HRQoL

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Background: To evaluate the quality of life related to satisfaction (HRQoL) and compliance in patients with moderate to severe atopic dermatitis (AD) in pharmacological treatment.
Method: Prospective local study with adult patients (16 to 70 years) diagnosed of moderate or severe AD of at least 12 months of evolution and in topical and systemic drug treatment. The Quality of Life Index in Dermatology (DLQI), the Scale of Affectation of Atopic Dermatitis (EADA), Hanifin and Rajka criteria for diagnosis and analog visual satisfaction scales were applied. HRQOL was compared between patients with moderate and severe involvement (Mann-Whitney U) and the duration and number of outbreaks before and after maintenance therapy (Wilcoxon test).
Results: 15 patients of both sexes of different ages participated: 5 (16 to 23 years), 7 (24 to 55 years), 3 (56 to 70 years);, with moderate and severe DA among the total cases. The impact on HRQOL was moderate in 80% of patients with moderate AD, while the impact on HRQoL was severe/severe in the total of patients with severe AD. The duration and number of outbreaks in patients with moderate AD, decreased from the application of treatment (topical and systemic), while patients with severe AD did not present significant changes compared to the application of the treatment, even in the 3.5% had an increase in the number of outbreaks.
Conclusion: Patients with moderate or severe AD who continue pharmacological treatment Topical and systemic maintenance present a reduction in the duration and number of outbreaks with consequent minor Affectation of your HRQOL. While those patients with severe AD with association to infectious agents do not present improvement of the DA in their treatment with the consequent severe affectation to their quality of life.

TP0991 | "I look disgusting"—A qualitative enquiry into the impact of atopic dermatitis on quality of life in adults

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Background: Atopic Dermatitis (AD) has been related to poorer health-related quality of life (HRQoL) in adults, but no qualitative research has been published to explore in any depth how this long-term condition affects the lives of adults. The purpose of this study was to explore the impact of AD on HRQoL of adults through semi-structured interviews.
Method: Adults with a clinical diagnosis of AD were recruited by advertising on a University campus and through social media sites. All completed a screening questionnaire on AD diagnosis, treatment, duration and severity. Semi-structured interviews were conducted, audio-taped, transcribed verbatim and analysed using thematic analysis.
Results: Participants (n = 19) consisted of ten White and nine Black and Ethnic Minority (BME) participants, aged 19-52; 18 were female. Five super-ordinate themes emerged from the analysis: visibility of AD; threats to inner sense of self; threats to physical capacity due to pain and management; developing confidence in management of AD; and social support. There were qualitative differences in the narratives of those who were diagnosed with AD at an early age compared to a later age, and across ethnic groups.
Conclusion: AD has a great impact on the QoL of adults. Participants in this study discussed issues that have not been reported in quantitative research, particularly lack of understanding of the psychological impact of AD, and the stigma attached to AD. Consideration of these factors may enhance disease management and improve HRQoL. Understanding and recognition of atopic dermatitis as a complex long-term condition involving significant psychosocial impact is crucial. Our findings suggest more integrated and accessible psychological support is required for people with AD. Men were under-represented in this study and further exploration of the impact on AD in men is needed.

TP0992 | Fullerene C60 aqueous dispersions exhibits anti-inflammatory activity in murine model of chemical burn

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Background: Aqueous fullerene C_{60} dispersions (AFD) and fullerene derivatives have proven to be potent anti-inflammatory

agents. Due to their low bioavailability, they seem especially prominent as a potential topical drug. Fullerene based preparations' efficiency has been established for treatment of atopic dermatitis, acne vulgaris, wounds and lesions and other skin ailments. This work explores effect of AFD on skin inflammation, caused by chemical burn.

Method: Female Balb/C mice aged 6-8 weeks were subjected to general ether anesthesia, during which a 2 × 2 cm region of skin has been shaved and a 1 × 1 cm cotton pad, wetted with 12.5 N sodium hydroxide solution was applied. Control mice received applications of phosphate buffered saline (PBS). Initial application was followed by a 14 day treatment period, during which an ointment, containing either AFD, d-panthenol (positive control) or PBS (negative control) has been applied daily to the damaged skin, and the burn area has been measured. Following necropsy on 15th day of therapy a complete blood count, histological study of damaged skin and q-PCR measurement of FGF-b, EGF,HMGB1, Hif-1a, TNFa, TGFb1, VEGF-A, IL-1a, IL-1b and IL-6 gene expression were performed. All animal handling procedures were approved by institute ethics committee.

Results: Visual evaluation, histological study and measurement of damaged skin surface area have shown that treatment with fullerene C_{60} containing ointment was comparable in its effectiveness with d-panthenol treatment. Complete blood count did not reveal pathological changes in any of the groups studied; however, a considerably lover amount of thrombocytes in the group, treated with AFD ointment compared to group treated with d-panthenol and untreated group has been observed. q-PCR analysis did not reveal many differences between "AFD" and "d-panthenol" groups, apart from slight dissimilarities in FGF-b, EGF and VEGF-A expression levels.

Conclusion: Fullerene C_{60} containing ointment has been found to improve skin condition and decrease inflammation in murine model of chemical burn caused inflammation. Its activity is comparable to that of d-panthenol, with some slight differences in thrombocyte and VEGF-A levels. Overall, AFD activity speaks to the promise of creating a new therapeutic agent for treatment of cutaneous burns.

TP0993 | Evaluation of the antioxidant defense of patients with atopic dermatitis

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Background: Our body has two systems of elimination of free radicals (FR): 1: Enzymatic, glutathione peroxidase (GPx), catalase and superoxide dismutase (SOD) and 2: Non-enzymatic, composed of vitamins A, C, E and trace elements such as zinc and copper. In addition, there is an important biomarker called malondialdehyde (MDA) to reveal a strong oxidative stress. Vitamins and trace elements are absorbed through a balanced diet, rich in fruits, legumes, eggs and fish. Atopic dermatitis (AD) is a chronic and recurrent inflammatory skin disease characterized by severe pruritus and eczematous lesions that usually begin in early childhood. The aim of our study was to evaluate the antioxidant mechanisms of AD pediatric patients in comparison to healthy children.

Method: Cross-sectional study carried out at the AD Referral Center. Sample size calculated to achieve a 95% confidence level (PASS 2008 software). AD patients (n = 48) and healthy children (controls, n = 25) - 2; 1, matched by age and sex, were compared by assessing the plasma concentration of vitamins A, C, E, SOD and MDA.

Results: Oxidative stress can be defined as an instability in the production of free radicals (FR) and antioxidant defense which results in injuries in all cellular components. AD patients appeared to be more prone to damage caused by reactive oxygen species (ROS) when compared to the control group according to our results: Vitamin C concentrations (median: patients: 34 *vs* control: 100 ng/mL = $P < 0.001$), zinc (median: patients: 94.5 *vs* control: 74 µ/dL = $P < 0.001$) and MDA (median: patients: 63 *vs* control: 25.04 nmol = $P < 0.05$) presented a statistically significant difference in AD patients compared to healthy children.

Conclusion: It is inferred that the increase in the prevalence of allergies can be motivated by the low intake of foods rich in antioxidants present minimally in ultraprocessed foods, among other factors. Therefore, an antioxidant nourishment can be used as adjunctive treatment in AD. An interdisciplinary team is critical in managing allergies in general. For this intervention, the action of a nutritionist becomes essential.

TP0994 | Eczema herpeticum on a tattoo

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Case report: The purpose: is to draw attention to rare cases of Kaposi varicelliform (eczema herpeticum) and their importance and approach in current practice.

Background: Kaposi varicelliform or eczema herpeticum is a viral eruption on a pre-existing cutaneous disease. Classically the

disorder is a Herpes Simplex type 1 virus infection occurring in a patient with atopic dermatitis. Lately corrections to the definition have been made, eczema herpeticum can be caused by other viruses such as *Herpes Simplex type 2 virus*, *Coxsackie A16*, *Vaccinia virus* or *Varicella zoster virus* occurring in a patient diagnosed previously with contact dermatitis, psoriasis, bullous dermatoses, Grover disease, mycosis fungoides, rosacea, seborrheic dermatitis, burns or skin grafts.

Method: We describe a case of eczema herpeticum, caused by Herpes simplex type 1 virus, appeared on a tattoo made on the superior limb.

Results: In favour of the diagnosis were:

clinical aspect: clusters of umbilicated vesicles and crusted lesions localized within the tattoo;

Tzanck smear was positive, confirming the viral etiology of the skin lesions and excluding allergy;

Patch test was interpreted negative;

DNA-PCR confirmed the herpetic etiology;

Antiviral therapy (systemic acyclovir) proved to be effective.

Conclusion: Eczema herpeticum affects people with atopic dermatitis and other inflammatory skin diseases; although rare, it is considered a potentially life-threatening disorder. The infection can be very serious, especially when it spreads over wide areas of skin, complications may include: severe scarring from blisters, keratitis, and even organ failure.

TP0995 | The 1196 C> T polymorphism of the TLR-4 gene and cytokine profiles in adults with extrinsic (exogenous) and intrinsic (endogenous) forms of atopic dermatitis

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Background: Some studies have shown that the 1196 C> T polymorphism of the TLR-4 gene may be associated with high levels of IgE and positivity of skin prick tests.

Method: The 1196 C> T polymorphism of the TLR-4 gene was studied in 96 patients with atopic dermatitis. The control group included 90 non-atopic volunteers. The single nucleotide polymorphism of 1196 C> T was detected by PCR. The levels of total IgE and TNF-α, IL-2, γ-IF, IL-4, IL-5, IL-10, TGF-β cytokines in blood were detected by ELISA Patients and volunteers provided written informed consent for the genetic study.

Results: 34 patients had exogenous and 62 had endogenous atopic dermatitis. In the control group, the frequency distribution of genotypes (CC – 84 (93.3%), CT – 6 (6.7%), TT – 0 (0%)) did not significantly differ from those with atopic dermatitis (CC – 85 (88.5%), CT – 11 (11.5%), TT – 0 (0%), $\chi^2 = 7.45$, $P = 0.024$). The homozygous TT genotype was not found in this population. Only 11 patients with atopic dermatitis and 6 volunteers had the heterozygotic genotype CT. Patients with the exogenous form of atopic dermatitis have a tendency towards increase in the prevalence of the heterozygous genotype CT (OR = 3.000, $P = 0.065$) in combination with an elevated level of total IgE and IL-2 in comparison to the control group.

Conclusion: The risk of atopic dermatitis development in this Ukrainian population is not associated with 1196 C> T polymorphism of the TLR-4 gene.

TP0996 | Capsaicin-induced atopic dermatitis-like symptoms were improved by suppression of NF-KB signal

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Background: Previously, we observed that capsaicin induced atopic dermatitis (AD)-like dermatologic symptoms in rats through dysregulation of proteolytic system. Capsaicin-induced AD-like symptoms were improved by our newly designed synthetic peptide NCP112O. NCP112O is a synthetic peptide designed on the basis of crucial region of a ligand for N-formyl peptide receptor 2 and antimicrobial peptides.

Method: To elucidate the underlying mechanism of capsaicin-induced AD model, proteomic analysis of cutaneous tissues was performed using capsaicin-injected rats. Also the results of proteomic analysis were confirmed by immunohistochemical staining of tissues.

Results: In proteomic analysis, expression level of several peptides including AMPs (S100A8/9 and cathelicidin) were increased in AD rats, which was decreased by NCP112O treatment. To analyze whether AD is related to the NF-kB signaling, AD group was treated with several NF-kB inhibitors. As a result, symptoms of AD model were mitigated by dexamethasone, Bay 11-7082 and NCP112O. NCP112O also inhibited NF-kB signaling related to production of AMPs and epidermal cytokines in AD group and HaCat cells. In immunostaining, the expression levels of epidermal cytokines and of AMPs were decreased in NCP112O-treated group. In addition, the expression levels and location of Lgr6, filaggrin, CDSN, KLK7 and matriptase within the epidermis improved with NCP112O treatment.

Conclusion: The result suggests that capsaicin activates NF-kB signaling to produce AD-like symptoms. NCP112O mitigates the manifestations of AD through suppression of NF-kB signaling.

TP0997 | Determinants of vitamin D deficiency in chilean children with atopic dermatitis

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Background: Vitamin D (VD) deficiency is common in children with atopic dermatitis (AD) and has been associated with severity of AD in several reports. However, there are no studies evaluating possible determinants of VD deficiency in children with AD. The purpose of this study is to evaluate determinants of VD deficiency in children with AD from Santiago, Chile.

Method: As a substudy of the VIDATOPIC trial, we used LC-MS/MS to assess baseline serum 25-hydroxyvitamin D (25(OH)D) concentrations in 101 children with active AD. All children were recruited between May and October of 2014. AD severity was evaluated by SCORing Atopic Dermatitis (SCORAD) index. Dietary intake of VD was evaluated with a food frequency questionnaire. Unadjusted and multivariable logistic regressions were performed to evaluate the associations of sociodemographic and clinical factors with VD deficiency defined as serum 25(OH)D < 50 nmol/L.

Results: 55% of children with AD had VD deficiency, with a mean 25(OH)D of 47 ± 20 nmol/l. Children with VD deficiency were significantly older than children with 25(OH)D > 50 nmol/L (7.4 ± 4.1 vs 4.8 ± 3.4 years, respectively; $P < 0.001$). Median VD dietary intake was 87 IU/day (interquartile range 42-141 IU) and was significantly associated with serum 25(OH)D (R^2=0.13, $P < 0.001$). 98% of children with AD received less VD than the Estimated Average Requirement of 400 UI/day. On unadjusted logistic regression, recruitment in spring season (OR = 4.8, $P = 0.008$), older age (OR = 1.2, $P = 0.003$), and screen time > 2 h/day (OR = 3.0, $P = 0.009$) were associated with VD deficiency, while VD dietary intake was a modest protective factor (OR = 0.99, $P = 0.004$). Multiple factors (e.g., gender, nutritional status, SCORAD, serum IgE, eosinophil count, Fitzpatrick skin phototype, asthma, food allergy, and sunblock use) were not associated with VD deficiency. In a multivariable logistic regression model, recruitment in spring season and older age were associated with VD deficiency (aOR = 8.8, $P = 0.006$, and OR = 1.2, $P = 0.001$, respectively), while dietary VD intake showed a modest protective effect (aOR = 0.99, $P < 0.007$).

Conclusion: Season, age, and dietary intake of VD are associated with VD deficiency in children with AD. Food fortification and supplementation with VD are potential preventive and therapeutic measures against VD deficiency in this population.

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TP0998 | The role of immunoglobulin, plasmapheresis and corticotherapy in the treatment of Stevens-Johnsons syndrome/toxic epidermic necrolysis

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Background: Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (NT) are rare mucocutaneous reactions that correlate with severity spectrums of the same disease. They are frequently triggered by drugs and the mucocutaneous reaction culminates in extensive necrosis of the epidermis. Nowadays, there is no defined treatment; however, its identification is essential in order to reduce its high morbidity and mortality.

Method: Retrospective, descriptive and inferential study of patients hospitalized in a tertiary hospital with the diagnosis of SJS/NET for 16 years, evaluating: age, sex, SHORTEN, burned body surface area (BBSA), C-reactive protein (CRP), procalcitonin (PCT), mucosal attainment, comorbidities (BMC), complications and mortality. The difference between the therapies in addition to the supportive treatment: systemic corticosteroid (CTC), human intravenous immunoglobulin (IVIG) and plasmapheresis (PLM) was analyzed.

Results: Fifty-eight patients were identified, mean age of 63.4 ± 20.0 years old, 58.6% female and 50% SCORTEN at admission greater than or equal to 3. There were 27.6% with SJS, 62.1% with NET and 10.3% with overlap. In 67.2% there were BMC and 25.9% corresponded to oncologic BMC. CRP was positive in 82.8% and PCT in 31.0%. Regarding the triggers, 67.2% was due to a single drug, 13.8% drug association and indeterminate in 19.0%. The drug most frequently involved was Allopurinol (32.8%) and the pharmacological group was antibiotics (32.8%). In 86.2% of the patients, the mucous membrane was affected, with the ocular mucosa being the most frequent (63.8%). The hospitalization time (INT) was 17.8 ± 21.2 days with a total mortality of 29.3%. Regarding therapy: 43.1% performed PLM (mean BBSA 51.7 ± 23.4%, mortality of 36%); 43.1% CTC (mean BBSA 21.1 ± 22.5%, 20% mortality) and 25.9% IGIV (mean BBSA 58.0 ± 23.3%, mortality of 33.3%), not exclusive. Statistically significant associations were established between: a) CTC and BBSA ($P < 0.001$), maximal PCR ($P = 0.02$); b) IGIV and BBSA ($P < 0.001$), duration INT ($P = 0.002$); c) PLM and BBSA ($P < 0.001$), oncological BMC ($P = 0.032$).

Conclusion: Conclusion: SJS/NET treatment remains uncertain, with a limited number of comparative studies. The choice of therapy in this population was mainly based on BBSA, with the use of PLM and IVIG in more severe patients, but a high mortality rate was maintained. IGIV was associated with a reduction in hospitalization time.

TP0999 | Steven-Johnson syndrome to allopurinol: Case report

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Case Report:

Introduction: The Steven Johnson syndrome (SJS) is a rare immune complex-mediated delayed hypersensitivity reaction. It presents in three different forms: a mild form called erythema multiforme, the main form and the severe form called toxic epidermic necrolysis (TEN). SJS is mainly a drug related disorder.

Case report: A 63-year-old woman with hypertension, type I diabetes, chronic renal insufficiency presented in the emergency department with a 2-week history of malaise, fever, generalized pruritus. One day before admission to our department she complained of palpebral and lips edema, pruritic macular rash extending from the face, trunk and extremities, sore mouth and diarrhea. She had started treatment with allopurinol (300 mg tablet/day) 2 weeks ago for hyperuricemia. Vital signs were normal (heart rate was 75/min, blood pressure 113/75 mmHg, respiratory frequency 18/min, oxygen saturation 98%) without any mucosal involvement. Laboratory tests during hospitalization showed the following results: white blood cell: 10200/14600/mm^3; glucose: 175/285 mg/dl; urea: 138/154 mg/dl; creatinine: 2.5/2.1 mg/dl; sodium 139/134 mmol/l; AST: 22/31U/L; ALT: 32/48U/; anti-ANCA screen negative. Chest x ray resulted normal, abdominal ultrasound showed right atrophic kidney. Steven Johnson syndrome was suspected. The presumptive cause was allopurinol. Allopurinol was immediately withdrawn, and a regimen of 100 mg prednisolone intravenously (i.v), ceftriaxone 1000 mg twice daily (as a prophylactic measure), fluid replacement, oral desloratadine twice daily was administered. The response to therapy was fast. Facial edema started improving on the 3d day. After 10 days of hospitalization and treatment the patient's skin lesions and laboratory findings resolved completely and she was discharged. Oral antihistaminic and antileukotriene were prescribed on discharge and stopped after 2 weeks according to the complete resolution of the clinical and laboratory findings.

Conclusion: Allopurinol is one of the drugs most commonly associated with SJS/TEN probably because of the off-label prescription for asymptomatic hyperuricemia. This case highlights, that prompt

recognition of the disease and management of the patient contributes in decreasing the morbidity and mortality of Steven Johnson Syndrome.

Amoxicillin-induced toxic epidermal necrolysis with a fatal evolution

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Case report: A 64-year-old female Caucasian patient was admitted to our emergency unit for widespread areas of denuded epidermis covering over 30% of the body surface. The truncal lesions were accompanied by oral and genital mucosal lesions. The lesions started to occur 2 weeks after a treatment with Amoxicillin for a respiratory track infection. The patient was also treated at that time with several vitamin supplements.

Based on clinical findings and drug history, the diagnosis of Amoxicillin-induced TEN was established. The severity of illness score (SCORTEN) at admission was 6. The patient was admitted in the intensive care unit and supportive care was initiated associated with immunomodulatory treatment with high-dose intravenous immunoglobulins and corticosteroids. The effectiveness of intravenous immunoglobulins could be explained by blocking Fas-mediated keratinocyte necrosis. The role of corticosteroids in slowing the progression of the disease is controversial. However, if marked inflammation is seen, they could be used for a short period of time and early in the disease course. This was the reason why we decided to associate systemic corticosteroid treatment.

Despite specialized care, the general status of the patient deteriorated progressively and died 15 days after admission.

Severe blistering drug reactions are often life-threatening, with a fatal evolution depending on the severity of illness score – less than 10% of patients with SCORTEN over 5 will survive.

Aminopenicillins are among those medications associated with an increased risk of causing TEN, but the risk is considerably lower than that of anti-infectious sulfonamides. Unfortunately, there are no reliable tests to certify that a given drug is responsible for the skin and mucosal involvement. This is the reason why that all possible involved drugs should be rapidly stopped. Besides this, excellent supportive care remains the most important part in the management of these patients. However, despite following these recommendations the evolution of the patients remains unpredictive.

TP1001 | Seven-months retrospective study on drug hypersensitivity reaction with emphasis on severe cutaneous adverse reactions (SCARs) in our tertiary allergology clinic

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Background: Drug hypersensitivity reactions (DHR) are defined as objectively reproducible symptoms or signs affecting different organs, generated by exposure to a drug at a dose tolerated by normal persons. Based on their chronology DHR can be classified as immediate and non-immediate. The skin is frequently involved and severe cutaneous adverse reactions (SCARs) are a special category of pretty rare, non-immediate DHR, carrying high morbidity and mortality. SCARs comprise Stevens-Johnson syndrome (SJS), drug rash with eosinophilia and systemic symptoms (DRESS) and acute generalized exanthematous pustulosis (AGEP). Frequent culprits are beta-lactams, anticonvulsants, nonsteroid anti-inflammatories, and allopurinol; however, due to the extensive and occasionally inappropriate use of medication, new drugs, and sometimes less typical presentation are emerging.

Method: A retrospective analysis of all DHR presenting in our Clinic from 05.2018 to 01.2019 has been carried out. Data collection was based on the clinical records of the Allergology and Dermatology Clinic and the Allergology Consultation Registry. Reactions were Classified as immediate or non-immediate and their severity was graded as mild, moderate or severe based on the EAACI and ICON Classifications.

Results: A total of 125 cases of DHR were encountered. Out of these 70.4% (n = 88) were immediate and 29.6% (n = 37) were non-immediate. 25% (n = 22) of the immediate DHR were severe compared to 35.13% (n = 13) non-immediate, corresponding to SCARs. The most frequent SCAR reaction was SJS 46.15% (n = 6), followed by DRESS 38.46% (n = 5) and AGEP 15.38% (n = 2). The overall most frequent culprit was vancomycin (n = 4; 3 DRESSs, 1 AGEP), followed by valproic acid (n = 2; 2 DRESSs), amoxicillin/clavulanate (n = 2; 1 SJS, 1 AGEP) and interestingly two quinolones (n = 2; 2 SJS) and riluzole (n = 1; 1 SJS). Most patients had systemic involvement such as acute renal disease (53.84%, n = 7), hepatic cytolysis (30.76%, n = 4), ascites and pleurisy (n = 1, AGEP). Of note, both SJS driven by quinolones presented initially with lipedema which was at first interpreted and treated as an immediate reaction by our colleagues at the Emergency Room.

Conclusion: Out of 125 patients presenting in our clinic with DHR, 13 had SCARs (10%) mainly induced by notorious drugs although some (15.38%), showed a rather particular clinical pattern and were associated with less known culprits such as quinolones.

TP1002 | A probable pediatric case of acute generalized exanthematous pustulosis due to metamizole

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Case Report:

Background: Acute generalized exanthematous pustulosis (AGEP) is a rare severe cutaneous adverse reaction (SCAR) mainly caused by drugs. It is characterized by a rapid development of hundreds of small, nonfollicular, sterile pustules over an erythematous base that normally spontaneously resolves with desquamation within two weeks. In most of the cases AGEP is accompanied by fever and neutrophilia. Drugs more frequently associated with AGEP are antibiotics, although it has also been related to viral infections, hypersensitivity to mercury and spider bites. To our knowledge, there has only been one described case of AGEP caused by metamizole in a 56-year-old patient.

Case report: We report a case of a 13-year-old female with mild allergic rhinoconjunctivitis who received an appendectomy intervention and immediately after received a first dose of intravenous metamizole with no side effects. She was administered a second dose of intravenous metamizole 42 hours later, and after three hours presented a pruritic and erythematous skin reaction located in the trunk, abdomen, armpit and groin. Two days later, hundreds of pinhead-sized pustules appeared over the erythematous skin areas that rapidly increased in size. Mucous membranes were not affected. Fever was not detected and laboratory findings showed a normal blood count. A skin biopsy was not performed. After receiving a 9-day systemic corticosteroid treatment and oral antihistamines, the lesions started to desquamate leaving a skin hyperpigmentation that completely disappeared within 3-4 weeks. Outside of the allergological study, the patient tolerated ibuprofen and acetaminophen after the reaction.

Methods and Results: We performed patch tests on the upper part of the patient's back with metamizole and acid acetylsalicylic that were negative at 48 and 96 hours. Skin prick tests (SPTs) and intradermal skin tests (IDs) with metamizole were performed on the volar forearm. SPTs were negative and IDs with metamizole at 0.4 mg/mL and 4 mg/mL were positive at 24 and 48 hours presenting a considerable skin erythema surpassing the area of the application site. Regarding the EuroSCAR scoring system for AGEP diagnosis, the patient presented a punctuation of 7 (probable diagnosis of AGEP).

Conclusion: We present the first case of probable AGEP caused by metamizole in a pediatric patient who tolerates other nonsteroidal anti-inflammatory drugs.

TP1003 | Characterisation of an acute localised pustular drug reaction

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Case report: Introduction: Acute Localised Exanthematous Pustulosis (ALEP) is a rare and poorly defined cutaneous drug reaction, thought to be the localised form of Acute Generalised Exanthematous Pustulosis (AGEP). We describe a case of ALEP, analyse the literature and propose diagnostic criteria to assist in the diagnosis of this condition. We hope to improve awareness and welcome discussion to improve characterisation of ALEP.

Results*:* Case report: A well 31 year old woman developed acute perioral non-follicular pustules within 24 hours of amoxicillin dental prophylaxis. She reported perioral discomfort "tightness" but no pain or pruritus. She took no other drugs and had previously tolerated amoxicillin. She had no personal or family history of psoriasis or atopy. Examination revealed well-demarcated perioral clustered 1-2 mm non-follicular pustules on a base of erythema and oedema. Microscopy and culture were negative. A diagnosis of ALEP was reached through localised distribution, temporal relation to amoxicillin and morphologic features of AGEP as per EuroSCAR criteria. Cessation of amoxicillin led to prompt resolution with desquamation at 48 hours, and hyperpigmentation at 5 days. The patient declined oral re-challenge. Patch testing was negative.

Literature review: 19 published cases of ALEP were identified (table 1): 74% involved the face. All reported cases had a temporal association to a drug: 58% with ß-lactams, 16% with NSAIDs. Mean age was 43 years, with female preponderance (77%). 42% reported systemic symptoms. Most reports described "typical" features (non-follicular clustered pustules on erythema); however, three publications reported "atypical" morphology (larger isolated follicular pustules) and one case did not specify features. These "atypical" cases (shown in bold in table 1) were also associated with later onset from drug exposure: 7-14 days, compared with < 72 hours, suggesting possibly distinct aetiology from "typical" cases.

Discussion: As a result of our analysis of all published cases of ALEP we propose diagnostic criteria for ALEP to improve speed and consistency of ALEP diagnosis:

Acute onset within 72 hours from a trigger drug
Resolution within 14 days of ceasing the trigger drug
Localised distribution of many small (1-3 mm), non-follicular pustules
Well-demarcated background erythema and oedema
Negative microbiology

TP1004 | Skin desquamation and onycholysis nonpigmenting fixed drug eruption caused by amoxicillin

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Case Report:

Background: Fixed drug eruption (FDE) is a delayed drug hypersensitivity reaction that rarely occurs in children. The most frequent drugs that cause FDE are analgesics, antimalarials, barbiturates and antibiotics including amoxicillin. There are rare clinical variants of FDE that include: nonpigmenting FDE (NPFDE), generalized FDE and other atypical presentations. NPFDE is characterized by not leaving any residual hyperpigmentation.

Case report: We report a rare case of a 17-year-old male teenager with Down Syndrome and mild atopic dermatitis, who presented four episodes of bullous skin desquamation on the posterior part of his thumb and index finger of his right hand 24-48 hours after finishing 7 days of oral amoxicillin treatment prescribed for infections such as tonsillitis. The first episode occurred at the age of 13 and reactions occurred in each of the following three years after the intake of amoxicillin. In one of the four episodes, the extension of the reaction also produced onycholysis in his right index finger that recovered spontaneously after a few weeks. In all the episodes the skin lesions disappeared without leaving any residual lesion within one week.

Methods and Results: We performed patch tests on the upper part of the patient's back with amoxicillin, amoxicillin/clavulanic acid, penicillin and cefuroxime, all of which were negative. Drug challenge test (DCT) with 750 mg of amoxicillin every 8 hours for 7 days was positive 48 hours after finishing the last dose, with the patient presenting bullous desquamation from the distal posterior part of his thumb and index finger. We also evaluated cross-reactivity to another beta-lactam by performing a DCT with 750 mg of penicillin G every 8 hours for 7 days, which was tolerated. Outside the allergological study, the patient was also prescribed cefuroxime, a beta-lactam with a different side chain, which was also tolerated.

Conclusion: We present a very rare case of skin desquamation and onycholysis nonpigmenting fixed drug eruption caused by amoxicillin in a teenager patient who tolerates other beta-lactams with a different side chain.

TP1005 | Delayed systemic hypersensitivity reaction due to mitomycin C

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Background: Mitomycin C is an alkylating chemotherapeutic agent that is instilled intravesically to prevent the recurrence of superficial bladder carcinomas. Eczematous skin reactions after intravesical instillation of mitomycin C due to delayed-type hypersensitivity reactions are described. However, allergic systemic reactions are very uncommon with two isolated case reports described.

Method: A-82 year-old male patient treated with intravesical mitomycin C for bladder carcinoma developed pruriginous erythematous lesions in forearms, legs and the lumbar region, from the fifth to the eighth chemotherapy cycle. During the previous four cycles he complained of generalized skin pruritus, without lesions. The patient did not improve with oral antihistaminics.

When he was evaluated in our Service, about one month after the last cycle, the patient complained of itch an presented erythematous plaques located in his forearms, legs and lumbar region. Patch tests with mitomycin C (0.2% pet and 0.8% pet) were performed in the back. The patient had no lesions and he was not receiving treatment at that time.

Results: We obtained a positive result with patch tests with mitomycin C (+++) in both concentrations (0.2% pet and 0.8% pet) at D2 and D4. As negative control, petrolatum was also patch tested with a negative result. A challenge test was not performed due to the characteristics of the drug and its administration.

Conclusion: Generalized eczematous reactions due to mitomycin C are very unusual. We present a case report of systemic dermatitis with delayed hypersensitivity to intravesical mitomycin C demonstrated by positive patch tests. Before presenting skin lesions the patient complained pruritus without skin lesions. This could be a warning symptomatology in patients receiving mitomycin C.

TP1006 | Cutaneous reaction after intravesical instillation of mitomycin C

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Case Report:

Background: The use of intravesical Mitomycin C administration for the treatment and prevention of superficial bladder cancer is associated with many side effects including the development of chemical cystitis, eosinophilic cystitis and cutaneous exanthemas (9%).

The most frequent skin conditions are dermatitis, which generally affects the limbs and, less frequently, the genitals and trunk. Dermatitis is presumed to result from a type IV hypersensitivity

mechanism, since positive patch tests with Mitomycin 0.1-1% have been observed.

Case Report: A 51-year-old woman currently in treatment phase with bi-monthly Mitomycin C instillations for recurrent superficial bladder cancer presents 48 hours after the first dose of Mitomycin C with localized pruritus, irritation and stinging near the administration area. Symptoms subsided spontaneously during the day.

Fifteen days her symptoms recur 24 hours after the second instillation of Mitomycin C this time with a similar but more intense reaction that takes longer to subside (2-3 days). Within a few hours after the third dose she develops vulvar pruritus and irritation, bladder pain, scalp pruritus and generalized pruritic papular erythematous lesions. Her reaction lasted several days without skin peeling or residual lesions. It was noted that prior to the administration of Mitomycin, Povidone Iodine and Chlorhexidine were applied as antiseptics. Interestingly twenty years ago, she received instillations of Mitomycin monthly for 1 year for the same pathology, and with the last dose had developed nonspecific skin involvement that resolved spontaneously.

Methods and results: Patch tests were performed with Mitomycin C, Povidone Iodine, Chlorhexidine.

Povidone iodine and Chlorhexidine results were negative.

Mitomycin C (0.1%, 0.3%, 1%):

Reading at 30 minutes: negative.

Reading at 48 and 96 hours: positive.

Conclusion: We present a case of a cutaneous reaction after intravesical instillation of Mitomycin C with the following characteristics:

First reaction 20 years before.

Initial reaction compatible with type IV hypersensitivity mechanism with late onset of symptoms.

The subsequent reactions were more immediate, with clinical signs of greater intensity and persistence, similar to an accelerated type.

In the reviewed literature, positive patch tests with 0.1-1% Mitomycin C are described. We recommend performing epicutaneous tests at the lowest concentration (0.1%).

TP1007 | Successful desensitization to anti-tuberculosis drugs in patients with delayed-type allergic reactions

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Case report Objectives: Although delate type reactions to anti-tuberculosis drugs are more frequent, both early and late type reactions have been reported. Delate type reactions reaction to anti-tuberculosis drugs include Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme, and drug rash with eosinophilia and systemic syndrome, Maculopapular eruptions, Fixed drug eruptions.

Method: Desensitization procedures were performed in 2 patients diagnosed with tuberculosis and had maculopapular eruptions to anti-tuberculosis drug.

Results: The drugs used for these procedures were isoniazid (n:2), rifampicin (n = 2), pyrazinamide (n = 2). 2 patients underwent resolution of the previous allergic reactions before desensitization. The median duration of desensitization was 5 days.

Conclusions: *Desensitization was successfully completed and patients could tolerate* isoniazid, rifampicin, pyrazinamide

Drug	Dose(mg) Day
INH	7.5
	15 1
	22.5
INH	37.5 2
	37.5
INH	50 3
	50
INH	75 4
	75
INH	150 5
	150

Drug	Dose(mg)	Day
PZA	7.5	1
	12.5	
	25	
	50	
	50	
PZA	150	2
PZA	300	3
PZA	600	4
PZA	1200	5

Drug	Dose(mg)	Day
RIF	6.5	1
	12.5	
	25	
	50	
RIF	100	2
RIF	150	3
RIF	300	4
RIF	600	5

TP1008 | Kounis syndrome type II despite premedication. A case report

Paulauskas Vasaitis RM; Gonzalez G; Palazuelos J; Montorodefrancisco A; Mateos-Galvan J; Coto-Morales B

Hospital Central de la Defensa, Madrid, Spain

Case Report:

Background: Iodinated Contrast Media (ICM) are substances used in radiographic procedures to enhance visibility of structures. Among several adverse reactions, there′s an entity described in 1991 by Kounis & Zafras called Kounis Syndrome (KS) or allergic coronary spasm, caused by a strong allergic reaction, three types have been described: I) coronary spasm, II) plaque erosion or rupture manifesting as acute myocardial infarction, III) coronary artery stent thrombosis.

Here we describe a case of KS type II due to ICM

Method: A 57-year-old man with a history of Hypertension, Diabetes, dyslipidemia, chronic ischemic heart disease, myocardial infarction (MI) 1998, unstable angina in 2008 that required four coronary bypasses, leg claudication at 300 mts with suspicion of critical iliofemoral stenosis and an adverse reaction to ICM more than twenty years before during a radiographic procedure with no clinical implications. Since he was prescribed with a computed tomography angiography (CTA) with the use of iobitridol to confirm the stenosis, he was referred to do an Allergy study which he refused, so he was prescribed with standard premedication and the use of a low osmolarity ICM if needed.

Result: The patient underwent the CTA with standard premedication previous to the study, feeling chest pain right after the infusion of the ICM that improved with oral nitrates, A few hours later the symptoms worsen so he went to the Hospital and was tested with cardiac biomarkers (troponin T:405,4 ng/l, CPK:509 U/L) diagnosed NQMI, Killip I, and had: 1) an echocardiography: that showed local contraction disturbance and reduced ejection fraction (LVEF: 30%) and 2) a coronary angiography: showing a generalized coronary artery disease, blocking of LIMA-LAD, RCA, SVG-OM2 and calcification of OM2.

Conclusion: Here we describe a KS type II due to ICM despite premedication. Since various mechanisms have been incriminated to explain the adverse reactions due to ICM, it′s very hard to exactly predict the possibility to have one, that's why there must be kept in mind whenever a radiographic procedure is indicated: 1) the personal risk factors, 2) the risk-benefit balance for each patient, to reduce exposures to potential dangerous interventions like in this case: a severe cardiac disease patient with a suspected adverse reaction to ICM.

TP1009 | Fixed drug eruption induced by meloxicam

Nuñez Hernandez MA; De Vicente Jiménez TM; Paulauskas-Vasaitis R; De Mateo Hernandez MB; Hernandez-Peña J

Hospital Central de la Defensa., Madrid, Spain

Case Report:

Background: In patients who are intolerant to non-steroidal anti-inflammatory drugs (NSAIDs), COX-2, both preferential and selective inhibitors, may be a valid alternative although they are not always well tolerated, so it′s necessary to perform an oral tolerance study before securely prescribing them. Objectives: Verify the safety of Meloxicam and Etoricoxib (a preferential and a selective inhibitor of COX-2, respectively) in a patient intolerant to multiple NSAIDs and corticosteroids.

Methods: An 89-year-old woman, referred to our Allergy Department by the Anaesthesiology Department pending breast cancer surgery, who has a clinical history of skin rash, hives and occasionally blisters with residual macular eruption, due to NSAIDs or analgesic treatments, including cortisone. The last adverse reaction to these drugs took place more than 10 years ago. No allergological study was performed in her country of origin and there is no information available about the drugs involved. She is known to tolerate Acetaminophen, Codeine and Tramadol. Controlled oral exposure to Etoricoxib and Meloxicam is performed after signing written informed consent.

Results: Etoricoxib 30 mg is shown to be well tolerated. Positive reaction to Meloxicam 7.5 mg: 8 hours after the exposure, she begins with itching and erythematous-violaceous macular rash in both left and right feet and calves evolving to blisters in the sole and outer border of feet. No fever or general symptoms associated. The reaction disappears after 2 weeks. She had a treatment based in: antibiotics, antihistamines and general blister care. Residual hyperpigmentation still remained in the same location as the previous reaction for more than 12 weeks.

Conclusions: We present a case of a fixed-bullous-symmetrical exanthema induced by Meloxicam in a NSAID-intolerant patient with tolerance to Etoricoxib. We emphasize the need to confirm the safety of these drugs through a controlled exposure study/challenge.

TP1010 | Symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) to spiramycin with tolerance to other macrolides

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University Hospital of Badajoz, Badajoz, Spain

Background: SDRIFE (Symmetrical drug-related intertriginous and flexural exanthema) is an acronym to identify an uncommon form of cutaneous reaction after a systemic drug administration with

affectation of intertriginous or flexural areas, with symmetry of affected areas and absence of systemic symptoms. It is most commonly associated to beta-lactams antibiotics, iodinated contrast agents and antihypertensive and chemotherapy drugs.

We report a case of SDRIFE to spiramycin with tolerance to other macrolides.

Method: A 76-year-old woman, with history of hypersensitivity to amoxicillin, who 7 days after a treatment with metronidazole and spiramycin, for a tooth infection, developed erythematous and itchy lesions in the bend of the elbows, and inframammary lines, without mucous membrane involving or any systemic symptoms. She was treated in the Emergency Department with antihistamines and corticosteroids improving within few days.

Results: Epicutaneous patch test with metronidazole and spiramycin with reading at 48 and 96 hours were negative. Skin Prick test and Intradermal test to these drugs were negative. An oral challenge test were performed before with metronidazole and after with spiramycin and therapeutic doses were subsequently taken at home for 7 days. Oral provocation test with metronidazole was negative, while the last day of spiramycin taking, she developed a pruritic and symmetrical erythema in armpits, popliteal and cubital fossa, submammary foldings and groins, without flaking or other symptoms. Three months later, epicutaneous patch test and skin prick test with azithromycin, clarithromycin and erythromycin were performed with negative results; additionally oral provocation test with these macrolides were well tolerated.

Conclusion: We presented a case of SDRIFE selective to spiramycin with tolerance to other macrolides.

In our case skin tests were negative and the oral challenge test was the only tool to ensure the diagnosis of SDRIFE to spiramycin after several days of treatment at home.

We have no found, in the published literature, another similar case of selective SDRIFE due to spiramycin.

TP1011 | Erythematous rash after treatment with amphotericin B

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Background: There are different groups of antifungals according to their chemical structure: polyene macrolides (amphotericin B and nystatin) azoles (fluconazole), allylamines, lipopeptides, pyrimidines and others. Liposomal amphotericin B (L-AMB) is used in the treatment of invasive fungal infections. L-AMB is also used for the treatment of Cryptococcal meningitis and mucormycosis. Most remarkable side effects of L-AMB are hypokalemia and renal insufficiency. Hypersensitivity with rash and pruritus has been described in rare cases.

Method: We present a case report of a-21-year-old patient with a personal history of type 1 diabetes mellitus, episodes of diabetic ketoacidosis and recurrent vaginal candidiasis. She had no history of atopy or previous drug reactions. During one of the diabetic ketoacidosis and systemic candidiasis episode, she was treated with intravenous amphotericin B and topical nystatin. After 12-14 hours of the last dose of amphotericin B and while in treatment with Nystatin vaginal cream, she presented itchy erythematous lesions in neck and chest that disappeared with dexchlorpheniramine. No desquamation was observed. She had previously tolerated amphotericin B. We performed skin prick tests, intradermal tests and patch test with amphotericin B with immediate and delayed reading. Open patch test and challenge skin test with nystatin cream were also performed, and, finally, an intravenous drug provocation test with amphotericin B was carried out.

Results: Skin prick and intradermal tests with amphotericin B with immediate reading were negative. Intradermal tests with delayed reading were negative. Patch tests with amphotericin and nystatin with reading at D2 and D4 were negative. Then the intravenous provocation test with amphotericin B was performed. It was negative in our outpatient clinic, but 24 hours later the patient presented an erythematous rash on face, arms and legs, that disappeared with cetirizine. The challenge test was repeated several weeks later with the same result. An open patch test and a cutaneous challenge test with nystatin cream were negative. Afterwards, the patient has tolerated fluconazole.

Conclusion: We present a case of exanthema due to amphotericin B, a polyene macrolide antifungal, with tolerance to other antifungal of the same group (nystatin) and to another of a different group (fluconazole, azole group).

TP1012 | Evaluation of diagnosis tests in patients with dress sindrome

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Case report: The Drug Reaction with Eosinophilia and Systemic Sindrome (DRESS), which pathogenesis is related to specific drugs, is clinically presented as an extensive mucocutaneous rash, accompanied by fever, hematologic alterations with eosinophilia, hepatitis, and possible affectation of other organs like kidneys, lungs and pancreas. The most frequent drugs involved are aromatic anticonvulsivants and allopurinol. In vitro methods are necessary to establish a diagnosis, especially given the low sensitivity of skin tests and the inherent risks of drug provocation testing.

Epicutaneous tests (ET) and lymphocyte activation test (LAT) are used for the diagnosis of the drugs implicated in DRESS in our population, being our objective to prove usefulness of ET and LAT in patients with RegiSCAR of at least 3.

Background: The Drug Reaction with Eosinophilia and Systemic Sindrome (DRESS), which phytogenesis is related to specific drugs, is clinically presented as an extensive mucocutaneous rash, accompanied by fever, hematologic alterations with eosinophilia, hepatitis, and possible affectation of other organs like kidneys, lungs and pancreas. The most frequent drugs involved are aromatic anticonvulsivants and allopurinol. In vitro methods are necessary to establish a diagnosis, especially given the low sensitivity of skin tests and the inherent risks of drug provocation testing.

Epicutaneous tests (ET) and lymphocyte activation test (LAT) are used for the diagnosis of the drugs implicated in DRESS in our population, being our objective to prove usefulness of ET and LAT in patients with RegiSCAR of at least 3.

Method: We have selected a group of seven women, with ages between 33 and 54, with compatible symptoms and score in the scale RegiSCAR > 3. The drugs initially involved were allopurinol, carbamazepine, antibiotics, NSAIDs and radiological contrast media (RCM) Every patient received ET, using vaseline or water, and LAT according to the technique of Beeler et al. with the drugs involved. Single Blind Placebo Controlled Oral Challenge (SBPCOC) was performed with alternatives or drug ET and LAT negatives.

Results: Patients with at least a score of 3 in the RegiSCAR were included in our study. A score of 3 was obtained in a patient; score of 4 and 5 in 3 respectively. The ET were positive to RCM (4), meropenem (3), carbamazepine (1) y el TAL was positive in MCR (3), meropenem (2), carbamazepine (1) allopurinol (1), amoxicillin (1) and piperacillin-tazobactam (1). In four patients ET and LAT were positive.

Conclusion: ET and LAT proved to be useful methods for the diagnosis of the DRESS syndrome in our population, being LAT slightly superior.

TP1013 | Allopurinol induced dress syndrome with renal involvement

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Case report: Background: Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is acute, potentially life-threatening, serious adverse drug reaction. It is characterised by fever, rash, lymphadenopathy, eosinophilia and/or other leukocyte abnormalities, and internal organ involvement. Very often it has a relapsing-remitting course despite withdrawal of the offending drug. Case presentation: We present a 71-year-old female who was referred to our Clinic for diagnostic evaluation. The patient was treated for gout with allopurinol for approximately 30 days, when she reported cough and fever up to 38 °C, along with abdominal maculopapular rash. During the next several days the rash affected all body surface area and edema of lips and eyelids appeared. The blood tests revealed eosinophilia (30%, 9.1 x10^9/l), leukocytosis (30 x10^9/l), elevated CRP (32.3 mg/l) and elevated liver enzymes-ALAT (116 U/L) and GGT (134 U/L). Ultrasound showed hepatomegaly. All other tests, including Hb, platelets creatinine, albumin, urea and total protein were within the reference ranges. Treatment with allopurinol was stopped immediately and patient received systemic corticosteroids. Her condition improved in the next few days and all abnormal blood tests returned within the reference ranges, except mild eosinophilia (0.5 x10^9/l). DRESS syndrome was diagnosed based on RegiSCAR criteria.

Two weeks later the patient returned at the Clinic with signs of exfoliative dermatitis, intensive pruritus, weakness. The following blood test abnormalities were found- eosinophilia (33.5%, 4.1 x10^9/l), mild leukocytosis (12.3 x10^9/l), elevated CRP (77.6 mg/l), anemia (Hb-97 g/L), decreased total protein (59 g/l) and albumin (31 g/l), elevated creatinine (288 μmol/l) and urea (14.3 mmol/L), hyponatremia (122 mmol/L). Liver enzymes were within the reference ranges. The patient was diagnosed with acute renal failure due to acute interstitial nephritis within the context of DRESS syndrome.

Discussion: The present case is most likely drug-induced hypersensitivity syndrome (DIHS)/DRESS syndrome induced by allopurinol intake. Despite discontinuation of the culprit medication, the patient experienced acute renal failure and re-occurrence of eosinophilia; therefore, appropriate follow-up is recommended once DRESS syndrome is suspected or diagnosed.

TP1014 | Lyell's syndrome in a female patient with multiple autoimmune disorders

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Case report: Lyell's syndrome, or toxic epidermal necrolysis, is a rare, potentially life-threatening mucocutaneous disease, usually provoked by the administration of a drug and characterized by acute necrosis of the epidermis. A 60-year old woman presented to our department with a 7-day history of generalised erythema, generalized desquamation, epidermolysis affecting trunk and proximal parts of extremities especially on gluteofemoral region, vasculitis in lower legs, and ulcerative lesions of buccal mucosa. She complained about high fever, weakness, generalised pruritus, dysphagia, pyrosis and pain on dexter coxofemoral articulation. The patient has been diagnosed with autoimmune gastritis and thyroiditis, and diabetes mellitus type 2 along recent months, as well as with bilateral coxarthrosis during actual hospitalisation. Ten days ago, she has been hospitalised at Department of Infectious Diseases because of high fever, and treated with levofloxacin and supportive therapy. Our supplemental anamnesis and documentation investigation revealed a previous allergic reaction to ciprofloxacin. Culprit drug withdrawal

(levofloxacin), administration of increased doses of prednisolone, and adequate doses of fluids, electrolytes and albumin leaded to attenuating of mentioned skin symptoms within 5 days. Ten days later, the skin got the normal appearance and the ulcerative lesions of buccal mucosa disappeared. Corticoid therapy is reduced gradually according to symptoms resolvement.

Conclusion: Our case demonstrated that Lyell's syndrome is a severe drug reaction; however, culprit drug withdrawal, corticotherapy and supportive measures can improve disease's outcome even in a patient with multiple autoimmune disorders. In addition, the careful allergist investigation can be the decisive measure on the detection of culprit medicament.

Laboratory data along hospitalisation are shown in the table below

Result of immunological tests	Anti TPO	Anti GPC	ANA	ANCAs	Anti-PR3	Anti-MPO
Positive	178 IU/mL	+ +	++++	133.6 U/mL	28%	31%
Negative	-	-	-	-	-	-

Parameters (normal ranges)	Day 1	Day 5	Day 10
WBCs/mm^3 (4.0-10.0) × 10^3	16.7 × 10^3	12.8 × 10^3	9.7 × 10^3
ERS (5-25) mm/h	40	32	19
CRP (1.10-8.00) mg/L	189	67.8	18
Total protein (6.0-8.3) g/dl	5.2	5.7	6.2

TP1015 | Delayed hypersensitivity reactions to adalimumab in a patient with rheumatoid arthritis successfully treated with immunoglobulin

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Case report: A 30-year old woman was admitted to hospital complaining of pain at injection site on right lower quadrant(RLQ) of abdomen. She was previously diagnosed as rheumatoid arthritis(RA) 3 years ago and maintained methotrexate, leflunomide and low dose prednisolone with pain controllers. She had no history of allergic diseases. The symptoms aggravated by her work and the laboratory test results revealed ESR 52 mm/hr, and RF 24.7 IU/mL. Adalimumab was administered on her RLQ of abdomen along with maintained medication. Seven days after administration of adalimumab, the rash on the injection site was developed and the patient presented to the clinic 12 days after the administration of adalimumab. The vital sign was stable but with body temperature 38.4°C. White blood cell was 1600 /uL with segment neutrophil 62.6%, and absolute neutrophil count was 1001.6/uL. Eosinophil at the time was 5.4%. Platelet 76 000 L and CRP was 0.2 UL/mL, RF 20.7 IU/L, and AST/ALT was 76/57 IU/L, and urinalysis and chest X-ray were clear. Total IgE was 88.8 IU/L, and *Dermatophagoides farinae* and *pteronyssinus* were within normal limits. She was isolated for neutropenia and referred to an allergist for delayed hypersensitivity reaction to adalimumab. As rash aggravated to her trunk and extremities, and developed abdominal pain and diarrhea, within two days of admission, immunoglobulin of 1 g/kg was administered for 3 days with systemic steroid and antihistamine. Fever subsided and generalized rash improved with CBC and LFT panel after 2 days after administration of IVIG. She was discharged from the hospital after a week from admission, and her CBC results completely improved with complete disappearance of rash.

Potential risk of delayed hypersensitivity reaction of adalimumab is written in label and to our knowledge, this is the first case in literature of delayed hypersensitivity reaction associated with adalimumab. The prompt recognition and treatment with IVIG lead to successful outcome of this patient and we suggest this should be the preferred course of a choice treatment in future cases.

TP1016 | Inflammatory side effect of an anti-inflammatory drug: Infliximab related leukocytoclastic vasculitis

Tunakan Dalgiç C

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Case report: Introduction: Infliximab is a chimeric monoclonal antibody to tumor necrosis factor (TNF). Hypersensitivity vasculitis (HV) is characterized by inflammation of the small vessels of the skin. Leukocytoclastic vasculitis (LV) is a histologic diagnosis. This deposition most commonly occurs secondary to drug reactions. We describe a patient with Ankylosing Spondylitis (AS) who developed HV with biopsy-proven LV with infliximab.

Case report: 31 year-old male patient has a history of AS for 1 year. He was refractory to treatment with colchicum dispert, methotrexate and mesalamine tablets, that is why anti-TNF was needed 6 months ago. The dose of infliximab is 5 mg/kg/cyclus with isoniazid tablets (100 mg/day) for prophylaxis. 8 days after his 5. therapy with infliximab, he developed painful, non-pruritic, palpable purpuric lesions on lower extremities. He had no other systemic symptoms, and not recently started any other new medications. He was referred to our outpatient clinic by rheumatologist on the fourth day of lesions. Physical examination revealed palpable purpura of the legs. Detailed laboratory investigation were normal. Skin biopsy resulted as LV. We prescribed topical steroids and antihistamines; systemic steroids were not preferred because he had no signs of systemic vasculitis. We could not perform drug

skin tests because drug intradermal and patch tests should be avoided for type 4 drug reactions.

Discussion: First of all, anti-tuberculosis drugs frequently result in cutaneous adverse reactions but isoniazid is known to have least toxic potential for cutaneous reactions. In contrast to tuberculosis related vasculitis, his vasculitis improve upon withdrawal of the suspected medication and can be controlled with the administration of antihistamines and corticosteroids. In addition, there was no evidence by history or examination to support an exacerbation of his underlying disease. On the literature isoniazid is a very rare culprit drug to cause LV so infliximab was thought to be the potential culprit. We advised him not to receive any other anti-TNF blocker due to the high cross reactivity and the potential fatal results of any recurrent vasculitis. During anti-TNF therapy, clinicians should always keep in mind the inflammatory side effects of anti-inflammatory drugs.

Note: Written informed consent has been obtained.

MONDAY, 3 JUNE 2019
TPS 23
RHINITIS: COFACTORS AND COMORBIDITIES

TP1017 | How to identify allergic rhinitis from danish registries: A validation study

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Background: Large-scale database/register studies can provide important data on prevalence, time trends, disease progression, comorbidities, and treatment of allergic rhinitis (AR). However, when conducting such studies, reliable identification of individuals with AR from databases is crucial. We aimed to assess the validity of eight different algorithms designed to identify adults with AR when used in Danish registers.

Method: Our primary definition of "true" AR was a positive serum specific IgE (≥0.35) and self-reported nasal symptoms retrieved from two general health examination studies conducted in adults (18-69 years) during 2006-2008 (n = 3471) and 2012-2015 (n = 7493). Secondary definitions of "true" AR was nasal symptoms only and self-reported physician diagnosed AR. The algorithms to identify AR were based on data two years prior to the date of the health examination and included prescriptions drugs (antihistamines and intranasal corticosteroids) or data on AR-related diagnoses from hospitals. We calculated sensitivity, positive predictive value (PPV), and corresponding 95% confidence intervals (95% CI) for each algorithm in the two time periods.

Results: Less than 45% of those we classified as having "true" AR (all definitions) had claimed a prescription for antihistamines or intranasal corticosteroids two years prior to the health examination, leading to low sensitivity. For all three definitions of "true" AR the algorithms with the highest validity were those requiring both antihistamines and intranasal corticosteroids. For the primary definition of AR: PPV = 65% (95% CI: 56%–73%) in 2006-2008 and PPV = 64% (95% CI 58%–74%) in 2012-2015.

Conclusion: Due to low use of prescription drugs among those defined as having "true" AR, the prevalence of AR will be underestimated when using Danish registers. Algorithms based on both antihistamines and intranasal corticosteroids had the highest validity. However, when applying a strict criterion for "true" AR (sIgE and nasal symptoms) 36% of those claiming both antihistamines and intranasal corticosteroids did not have "true" AR.

TP1018 | Investigation of allergic rhinitis epidemics by Baidu index in China

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Otorhinolaryngology Hospital, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Background: Allergic rhinitis (AR) is a common disease seriously affecting quality of life of patients. However, China lacks a traditional surveillance system to monitor the epidemics of AR. Baidu is the largest searching engine in China. Baidu Index is a web-based tool to investigate search volume (SV) of specific queries. Thus, we asked whether Baidu Index can reflect the epidemiology of AR in mainland China.

Method: We investigated the seasonal and regional pattern of SV of AR and related search terms in China. Then, we investigated the correlation of SV of AR and related search terms with real-world data including pollen count and outpatient visit volume.

Results: SV of AR showed repetitively seasonal pattern, with the first peak in May and the second peak from August to September. SV of AR in northern China was correlated with both SV of pollen allergy and dust mite allergy (all $P \le 0.001$). In southern China, SV of AR showed significant correlation only with SV of dust mite allergy (all $P < 0.001$), but not with SV of pollen allergy (all $P > 0.05$). The pollen count in Beijing was positively correlated with SV of AR ($r = 0.692$, $P < 0.001$) and pollen allergy ($r = 0.713$, $P < 0.01$). SV of AR in Guangzhou was closely correlated with the outpatient visit volume of AR (one month later, $r = 0.523$, $P = 0.001$ and two months later, $r = 0.503$, $P = 0.002$) in the First Affiliated Hospital of Sun Yat-sen University.

TABLE 1. Correlations between SV of AR and SV of Pollen allergy and dust mite allergy

	SV of AR and SV of pollen allergy		SV of AR and SV of dust mite allergy	
Region	r	P	r	P
China	0.348	0.006	0.722	<0.001
Northeast China	0.533	0.001	0.638	<0.001
North China	0.609	<0.001	0.791	<0.001
Northwest China	0.517	0.001	0.682	<0.001
East China	0.110	0.523	0.897	<0.001
Central China	0.171	0.319	0.884	<0.001
South China	0.020	0.909	0.799	<0.001
Southwest China	0.265	0.118	0.937	<0.001

Definition of abbreviations: AR = Allergy Rhinitis; SV = Search Volume. Correlation was examined using the Spearman's method.

TABLE 2. Correlations between pollen count and SV of Pollen allergy and AR

	Pollen count and SV of Pollen allergy		Pollen count and SV of AR	
Time lag	r	P	r	P
The same day	0.694	<0.001	0.692	<0.001
One day later	0.713	<0.001	0.651	<0.001
Two days later	0.691	<0.001	0.647	<0.001

Definition of abbreviations: AR = Allergy Rhinitis; SV = Search Volume. Correlation was examined using the Spearman's method. Time lag meant the time SV of pollen allergy or SV of AR lagged behind pollen count.

TABLE 3. Correlation between outpatient visit volume and SV of AR

Time lag	r	P
The same month	0.238	0.162
One-month delay	0.523	0.001
Two-month delay	0.503	0.002
Three-month delay	0.221	0.217

Definition of abbreviations: AR = Allergy Rhinitis; SV = Search Volume. Correlation was examined using the Spearman's method. Time lag meant the time outpatient visit volume lagged behind SV of AR.

Conclusion: Big data collected from Baidu index may reflect the epidemiology of AR in a nearly real-time manner, and broadcast the pollen season.

TP1019 | Ambrosia pollen count correlated with pediatric hay fever symptoms in Kyiv, Ukraine

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Background: This study was done to establish the relationship between symptoms and pollen levels during the *Ambrosia* season in children in Kyiv, in the north-central region of Ukraine.

Method: Patients sensitized to *Ambrosia* pollen from Kiev and Kiev region (N = 40) aged from 7 to 18, 65% male, 35% female, average age 13.7 years were examined during the years 2016-2018. Skin prick tests including *Ambrosia* prick as was sIgE to the leading inhalation allergens. Patients completed diaries on control of symptoms of rhinitis and conjunctivitis. During the exacerbation period, when the symptoms of rhinitis were more than 4 points, patients were prescribed loratadine; if the symptoms were higher than 8 points; loratadine and mometasone were prescribed, 2 sprays in each nostril; if conjunctivitis symptoms were more severe, olopatadine was recommended. Pollen counts were obtained from July 1 to October 31 using the Rotorod sampler maintained on the roof of Center of Allergic Diseases of Upper Respiratory Airways, Kiev, Ukraine, 12 m above the ground.

Results: There were no any significant correlations between pollen load and symptoms in 2016 but the ragweed season was generally low with the symptoms of rhino-conjunctivitis not exceeding 6 points. In both 2017 and 2018 seasons a correlation at a moderate level (0.4 and 0.5 ($P < 0.05$) respectively) was seen between the symptoms and rhino-conjunctivitis scores. This correlation was strongest during the first fortnight of September of both years, when children went back to school from and ragweed pollen counts were high.

Conclusion: This study of children sensitized to ragweed in Ukraine is the first one showing a correlation between symptoms and the ragweed pollen count in the Kyiv region.

TP1020 | Does new sensitisation correlate with nasal symptoms in children with allergic rhinitis?

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Background: New sensitisation is considered an indicator for worse prognosis in patients with allergic rhinitis. However, there is a lack of knowledge about the direct correlation between newly sensitised allergens and the development of allergic symptoms. Thus, this study aimed to evaluate the correlation between the increased number of sensitised allergens and nasal symptoms in patients with allergic rhinitis who were sensitised to house dust mite (HDM).

Method: Among the patients who were enrolled in the Allergic Rhinitis Cohort Study for Kids, 174 children who had rhinitis symptoms and were sensitised to HDM were included in the analysis. Skin prick tests, serum total immunoglobulin E, eosinophil count, and bronchial provocation tests were carried out during the initial visit and 3-year follow-up. A total of 62 patients were treated with sublingual immunotherapy (SLIT, mean duration of 2.3 years), and 112 patients were treated with pharmacologic therapy alone. The patients were divided into two groups depending on the change in the number of sensitised allergens: increased number of sensitised allergens (group I) and maintained or reduced number of sensitised allergens (group II).

Results: In the analysis of allergen sensitisation from the baseline to 3-year follow-up, no significant correlation was observed between the changes in the number of allergens and total nasal visual analogue scale score (R^2<0.001, $P = 0.813$). Furthermore, the comparison of

demographic data and immunological factors between groups I and II did not show any significant difference. The changes in bronchial hyper-responsiveness was not significantly different between the two groups (P = 1.000).

Conclusion: New sensitisation may not be correlated with nasal symptoms in patients in Asian countries where HDM plays a major role as a dominant allergen. Although further investigation must be conducted, the importance of new sensitisation as an indicator of treatment outcome should be reconsidered in individuals in Asia.

TP1022 | Prevalence of allergic diseases in adolescents according to gender

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Background: The prevalence of asthma and allergic rhinitis (AR) remains high and is still increasing in developing countries. Considerable sex-specific differences in the prevalence of allergic diseases have been observed.

Method: ISAAC written questionnaires were filled by 4520 adolescents 13-14 y/o from Curitiba, Brazil. Specific questions of allergic conjunctivitis (more than three episodes of itchy eyes in the last 12 months)previously validated were added to the ISAAC questionnaire. Four hundred and seventy-two participants were submitted to skin prick tests (SPT) with a panel of common regional aeroallergens and also answered a supplementary questionnaire on allergy risk factors.

Results: Of the 4520 participants, 2129 (47.1%) were boys and 2391 (52.9%) were girls. The overall prevalence of asthma was 17.5% (boys 14.6%, girls 20%; P < 0.01), AR 34.7% (boys 28.2%, girls 40.4%; P < 0.01), allergic rhinoconjunctivitis (ARC) 20.1% (boys 14.8%, girls 24.8%; P < 0.01), atopic dermatitis (AD) 5.9% (boys 5.4%, girls 6.3%; P = 0.26) and allergic conjunctivitis (AC) 15.5% (boys 13.3%, girls 17.4%; P < 0.01). The rate of sensitization to *D. pteronyssinus* in boys was 68.5% and in girls was 52.8% (P < 0.01), and to *B. tropicalis in* boys was 66.7% and in girls 48% (P < 0.01). Polysensitization rate was also higher in boys (P < 0.01).

Conclusion: Asthma, AR, ARC and AC were more prevalent in adolescent girls. Girls had more naso-ocular symptoms, even though they were less sensitized to inhalant allergens.

TP1023 | Self-assessed prevalence of allergic rhinitis among university students in Yerevan

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Background: It is very important to study the allergic rhinitis (AR) among students having their unique place in the population because the peak of AR prevalence falls on the 15-24 age group and the daily disturbing symptoms of AR lead to decrease in physical, mental and social activity, cause sleep disorders and sharp decrease in the quality of life. Thus, the aim of our research was to study the self-assessed prevalence of AR among university students in Yerevan.

Method: The questionnaire-based survey was performed among students in six different randomly chosen universities of Yerevan. 4126 completed questionnaires were given back (response rate - 84.9%) and 4071 (98.7%) were suitable for analysis. The study was approved by Committee of Bioethics of YSMU.

Results: 985 (24.2%, n = 4071) of students (371 male and 614 female), with mean age of 19.1 ± 1.2 have reported the presence of allergic upper-respiratory (sneezing, rhinorrhea, nasal congestion, itching) and/or eye (redness, tearing, itching) symptoms. The following concomitant symptoms were reported by students (n = 985): lower-respiratory (coughing, wheezing, etc.) - 239 (24.3%), skin (eczema, urticaria, itching, edema, etc.) - 386 (39.2%), oral (itching, salivation) – 68 (6.9%) and anaphylactic - 58 (5.9%).

The following factors were mentioned as a reason (n = 985): sun – 397 (40.3%), pollen – 331 (33.6%), dust - 291 (29.5%), smog - 242 (24.6%), smells - 225 (22.8%), weather – 183 (18.6%), animals - 43 (4.4%), unknown – 61 (6.2%). 288 (29.2%) of students have mentioned the food as a reason of associated (mainly skin and oral) symptoms.

417 (42.3%) of students have noted a connection of their symptoms with a certain year time and 71 (7.2%) – presence of symptoms all year round. It was revealed that the season lasts mainly 2-4 months, the peak of beginning falls on May and the peak of ending – on August.

380 (38.6%) of students have visited a doctor about allergic manifestations, 306 (31.1%) – have taken a treatment. The diagnosis of AR was verified in 126 (12.8%) of students, including 30 (23.8%, n = 126) with associated asthma and/or atopic dermatitis, and 11 (8.7%, n = 126) with food allergy.

Conclusion: The self-assessed prevalence of AR is high but the rates of visiting a doctor and consequently diagnosed allergy are very low. It is clear that although the students really understand that their allergy can be depended on season they have the stereotypic imaginations about the possible reasons of AR that is due to lack of information by our opinion.

TP1024 | Evaluation of olfactory function in children with vernal keratoconjunctivitis

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Background: Vernal keratoconjunctivitis (VKC) is a chronic and severe allergic disease of the eye, which characteristically affects boys in early to mid childhood living in hot, dry, subtropical climates. Symptoms consist of eye itching, tearing, mucoid discharge, redness, foreign body sensation, blurring of vision, photophobia and blepharospasm. Both IgE- and non-IgE-mediated hypersensitivity reaction play role in the pathogenesis and other systemic allergies, such as asthma and allergic rhinitis might be associated approximately in half of the patients. The aim of the present study is to assess olfactory dysfunction in pediatric patients with VKC in comparison with healthy children and correlate the results with acoustic rhinometry measurements.

Method: Forty-three children, diagnosed as VKC and 26 healthy children without atopy were enrolled in the study. After ophthalmological examination, endoscopic nasal examination, acoustic rhinometry, and Connecticut Chemosensory Clinical Research Center (CCCRC) tests were performed.

Results: VKC group included 27 male (62.8%) and 16 female (37.2%) with a mean age of 10.95 + /-3.2 years (range 5-18 years) and control group included 26 male (81.3%) and 6 female (18.8%) with a mean age of 11.69 + /-2.2 years (range 8-18 years). Thirty one % of the patients had tarsal type VKC, while 4 had limbal and 8 had mixed type. Allergic rhinitis was detected in 7 of the VKC subjects. There was no statistically difference in mean odor threshold between the healthy and vernal children (7.9 + /- 0.25 and 7.6 + /-0.69, respectively, $P = 0.087$), while odor discrimination and MCA were lower in vernal children (6.05 + /- 1.02 and 0.30 + /-0.15) than healthy subjects (7.06 + /-0.77 and 0.41 + /-0.16) ($P = 0.001$ and 0.019, respectively). Acoustic rhinometry parameters and odor threshold and discrimination did not differ according to vernal subtypes ($P > 0.05$). There were no correlations between acoustic rhinometry parameters and olfactory functions ($P > 0.05$).

Conclusion: We found a decrease in odor identification and MCA in children with VKC, while odor thresholds were not different. Children with VKC should be consulted with otolaryngologists for possible association of allergic rhinitis and olfactory dysfunction.

TP1025 | Validation of EQUICK – an electronic tool in english for monitoring symptoms of vernal kerato-conjunctivitis

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Background: Vernal Kerato-Conjunctivitis (VKC) is a severe allergic eye disease for which no validated symptom monitoring tools exist in English. eQUICK, an English electronic adaption of validated Italian quality of life score (QoL) score (QUICK[1]), was verified against three parameters, routinely used in our clinic. These are modified Juniper's QoL (RCQoL), modified 5-5-5 score[2] (m5-5-5), with ocular examination findings, & (Biswas And Sharma) medication score (BASMED), apportioning higher score to potent steroids.

Method: 11 children with VKC, attending our clinic were asked to report, RCQoL and eQUICK score. These, with BASMED & m5-5-5 score were recorded in our database at two separate visits & analysed.

TABLE 1 Parameters collected from patients at two separate clinic visits

Patient	RCQoL Visit 1	RCQoL Visit 2	?	eQUICK Visit 1	eQUICK Visit 2	?	5-5-5 Visit 1	5-5-5 Visit 2	?	BASMED Score Visit 1	BASMED Score Visit 2	?
a	12	1	-11	36	21	-15	10	300	290	24	164.8	140.8
b	87	47	-40	51	34	-17	23	23	0	270.4	40.4	-230
c	63	9	-54	38	21	-17	20	2	-18	72.6	106	33.4
d	64	16	-48	44	24	-20	244	121	-123	252.4	262.4	10
e	13	89	76	31	47	16	11	211	200	20.3	70.3	50
f	13	14	1	23	20	-3	1	2	1	2.8	22.6	19.8
g	116	113	-3	51	44	-7	223	123	100	60.4	101.2	40.8
h	112	27	-85	39	28	-11	11	1	-10	2.5	2.5	0
i	29	29	0	28	31	3	1	1	0	2.4	2.4	0
j	96	27	-69	44	38	-6	121	12	-109	82.6	42.6	-40
k	101	34	-67	42	31	-11	23	23	0	2.6	2.6	0

Results: Both RCQoL & eQUICK scores, reflected eye disease synchronously. The co-relation co-efficient was 0.75. Improved symptoms with increased medication, was noted in 50%. In cases j & b, both eQUICK and BASMED scores improved. For e, despite increased medication, eye symptoms remained sub-optimally controlled. Synchronicity between eQUICK and m5-5-5 score occurred in 50%. Case e showed poor m5-5-5 and worsening eQUICK score. Case a, atypically reported improved eQUICK despite, worsening clinical findings on m5-5-5. Cases f, k, b had no change in 5-5-5 scores but improved eQUICK scores. They reported improvement on the 2nd visit when ocular findings like cobblestones, though improved in appearance, still persist. We found eQUICK questionnaire to be effective in capturing symptoms of children with VKC. The electronic platform & pictorial representation of symptoms, is easier for children to use.

Conclusion: Both eQUICK & RCQoL show correlation in the majority of patients. RCQoL showed a larger magnitude effect in those with greater nasal symptomatology. eQUICK captured changes more than RCQoL in those with predominantly ocular symptoms. We believe that in children with predominant ocular symptoms of VKC, eQUICK is a useful reporting measure and may be an additional tool in future controlled trials. A larger sample analysis will be helpful to confirm these initial finding.

References: 1. Sacchetti M et al. Am. J Ophthalmol 2007;144:557-63; 2. Shoji J, Inada N, Sawa M. Allergology Intern 2009;58:591-.7

TP1026 | Tacrolimus 0.1% eye-drops in Vernal Kerato-Conjunctivitis refractory to cyclosporine: Our experience

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Background: Vernal Kerato-Conjunctivitis (VKC) is one of the most severe ocular allergic diseases and its treatment is usually "aggressive" because of frequent corneal complications. Mainstay of VKC therapy is topical cyclosporine given at different percentages, unfortunately some cases do not respond to this treatment. Recent trials showed the efficacy of Tacrolimus 0.1% eye-drops in refractory cases which were previously long-term treated, although complications, with topical steroids.

Purpose of our study was to assess the efficacy in VKC refractory cases, of Tacrolimus 0.1% eye-drops administration (2 times a day for 6 months) to treat refractory-to-topical-cyclosporine cases.

Method: *Patients and methods* In this retrospective study, 12 children of both sexes (8 males and 4 females), under the age of 10 years (mean age 7.3 years) were included, they were affected by VKC seasonal forms refractory to conventional treatment. These patients underwent, from April to September 2018, Tacrolimus 0.1% galenical eye-drops treatment after discontinuation of all previous topical treatments (artificial tears were the only drugs permitted).

Assessment of symptoms (itching, foreign body sensation and redness) and signs (punctate keratopathy, Trantas nodules and giant papillae) was carried on at T_0(baseline), T_1 (1 month), T_3 (3 months) and T_6 (6 months).

Results: Our study showed a statistically ($P < 0.001$) significant improvement in symptoms and signs we analyzed at T_1 examination which was maintained until last examination (T_6). The treatment was well tolerated and no side-effects or infections were registered.

Conclusion: In conclusion, 0.01% topical (eye-drops) tacrolimus administration showed efficacy and safety in management of refractory-to-cyclosporine VKC eyes, displaying the importance of anti-inflammatory and anti-allergic properties of this drug.

TP1027 | Impact of psychological traits on perceived severity of hay fever

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Background: Severity of allergic rhinitis (AR) is assessed by the influence of AR symptoms on work/school and other activities, presence of sleep impairment and/or bothersome symptoms. Objective measurement of disease severity are needed to better assess disease severity and efficacy of treatment. In this study, we investigated the correlation of allergic rhinitis severity as perceived by the patients and biomarkers of allergic response. We also investigated the correlation of perceived severity and some psychological traits that describe patients' personality.

Method: We included 39 patients with positive skin prick test with grass pollen extract. Biomarkers of allergic response included titrated skin prick test, grass pollen specific IgE levels and *in vitro* basophil activation test (BAT) with grass pollen. Severity of AR was assessed with questionnaires about AR symptoms and medication use during the grass pollen season. Combined symptom and medication score was also calculated. Influence on the quality of life was assessed with mini Juniper RQLQ. Psychological traits were assessed with The Big Five Inventory questionnaire, Body conciseness scale and The Kentucky Inventory of Mindfulness Skills Assessment.

Results: We didn't detect significant correlation between symptom score, medication score, combined symptom/medication score or mini RQLQ score and skin prick test wheal size, titrated SPT, sIgE levels or BAT results. On the other hand, there was a correlation between symptom score and private body consciousness ($r = 0.51$ $P < 0.001$), symptom score and neuroticism ($r = 0.41$, $P = 0.01$), combined symptom and medication score and emotions

scale (r = 0.34, P = 0.04), mini RQLQ score and emotions scale (r = 0.35, P = 0.05), and mini RQLQ score and observing (r = 0.42, P = 0.022).

Conclusion: Some psychological traits influence severity of AR as perceived by the patients and should be addressed in future studies to determine the best objective biomarker of AR severity.

TP1028 | MP-AzeFlu improves quality of life of patients with allergic rhinitis

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Background: Allergic rhinitis (AR) comprises a variety of symptoms affecting the nose, such as congestion, itching, rhinorrhea, sneezing, and loss of smell. Additionally, AR is frequently accompanied by ocular symptoms, such as itchy or watery eyes and redness. Severity of disease can have a profound impact on quality of life (eg, sleep disorders, emotional problems, impairment in activities of daily life, or social functioning), as well as on work productivity and school performance. MP-AzeFlu has been proven to be effective for the relief of AR symptoms; however, its impact on patient quality of life under real-life conditions had not been examined.

Method: An observational study to evaluate the use of MP-AzeFlu in different AR patient phenotypes (MeDALL) was conducted. This is the German part of a multinational, multicenter, prospective, noninterventional study designed to assess quality of sleep, as well as troublesomeness in daily activities (work and social), in routine clinical practice by Visual Analogue Scales (VAS). Patients with moderate-to-severe seasonal or perennial AR (VAS ≥ 50 mm) presenting with acute symptoms on inclusion day, for whom MP-AzeFlu has been prescribed for the first time and according to the summary of product characteristics and patient information leaflet, were included. Patients recorded their sleep quality and troublesomeness in daily activities as a result of their AR symptoms on the printed VAS provided in a patient card at the appropriate range (not at all troubled = 0; extremely troubled = 100 mm). Patient cards were collected for 446 patients at Day 0 (inclusion visit), 434 at Day 7, and 386 on the last day (≈Day 14).

Results: At baseline, patients reported VAS scores of about 60 mm for sleep quality, daily work, social activity, and outdoor activity. Day 7 patient cards revealed improvements in sleep quality and daily activities (all VAS ~34 mm) as a result of less AR symptoms. Similar results were reported at Day 14 with VAS scores of ≈ 27 mm. All patients reported a decrease of more than 33 mm VAS score in the troublesomeness of AR in all of the quality of life indicators assessed.

Conclusion: Use of MP-AzeFlu to relieve symptoms of AR improved patient quality of life as indicated by less troubled sleep quality and improvement in activities of daily living.

TP1030 | The importance of patients' residence in the evaluation of inflammation in allergic rhinitis

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Background: Allergic rhinitis (AR) is one the most frequent diseases of the modern world. More than half of the european people live in urban areas. According to recent studies exposure to airborne pollution change and aggravate clinical picture of AR. We aimed to investigate the clinical and immunological aspects of AR in patients living in urban areas.

Method: Our study included 65 patients with AR and 38 controls. All patients were adults (age over 18 years) and were enrolled in an outpatient clinic from an European capital: Bucharest. Mostly of them lived in an urban area (59 patients and all of the controls). Allergic sensitization was evaluated using skin prick tests for respiratory allergies (dust mites, animal dander, cockroach, rusts, pollens) in concordance with European Academy of Allergy and Clinical Immunology recommendations. Immunological investigations included the evaluation of interleukins: 1β,4,6,10,13,17, IFN-γ, TNF-α and total specific IgE. All patients signed informed consent and the study was approved by the local Ethical Committee. Statistical analysis was performed using SPSS20.0 programme with Man-Whitney test and Pearson's correlation test. $P \leq 0.05$ was considered as statistically significant.

Results: We have noticed a strong association between living in an urban area and IFN – γ (r = 0.038, P = 0.000) and total specific IgE (r = 0.000, P = 0.000). Same association was noticed between living in an urban area and a marker of allergic sensitization: the size of skin prick test (r = 0.019, P = 0.000). Some clinical aspects of rhinitis are correlated with urban residence: nasal obstruction (r = -0.290, P = 0.003), sneeze (r = -0.229, P = 0.019). It was also noticed a correlation between the levels of IL-17 and urban exposure (r = 0.234, P = 0.045).

Conclusion: Patients living in large urban areas presents particular aspects of AR. Urban pollution (that raises the levels of IFN-γ and IL-17 in exposed populations, including allergic patients) must be taken into account when allergists evaluate patients with AR.

TP1031 | Serum allergen-specific IgE in patients with rhynitis classified according ARIA

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Background: It is known that the production of serum IgE decreases with age of patients. The quantitative levels of specific IgE are not always correlated with the severity of the disease. In this study we analyzed the possible impact of age and disease severity in the group of respiratory patients.

Method: 102 patients (41 males and 61 females, mean age 40, sd 15) were enrolled in this study. All patients were tested by *in vivo* and *in vitro* tests for specific IgE for perennial and seasonal allergens. The severity of the symptoms was assessed by ARIA criteria and by virtual scale (VAS) in all patients. Relations among ARIA score, age and specific IgE were assessed fitting multinomial logistic regression models.

Results: Serum IgE levels decreased with age (Pearson r = -0.29 $P < 0.01$) and were unlinked with VAS (r = 0.09). Levels of specific IgE in patients with severe/persistent form, according to ARIA criteria (153 sd 226), were significantly higher than in patients with the intermittent mild form (33 sd 71, P = 0.015). The former patients were also younger (28.5 sd 9 years, vs 44 sd 16 in the intermittent/mild form) (P = 0.002). The relation between persistent/severe ARIA score and higher specific IgE remains also after correcting for age (P = 0.05).

Conclusion: Allergen specific IgE levels tend to reduce with age but are increased in the persistent severe form.

TP1032 | The nasal congestion reasons in topical nasal decongestants abuse patients

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Background: The topical decongestants (TD) are used very often in pediatric practice especially in nasal congestion cases. But in some cases efficacy of TD is arguable. The aim of our research was to evaluate the reasons of TD abuse.

Method: The TD abuse patients were under our observation. The ENT-endoscopy was performed in all cases, allergological tests were performed in cases it was needed.

Results: 135 TD abuse patients aged from 1 to 15 years old were examined by ENT doctor. 57 of them (42.2%) were directed to pass allergitests on the basis of anamnesis vitae and the diagnosis of allergic rhinitis was confirmed in 30 cases (22.2%). In other cases the reason of nasal congestion was: nasopharyngeal tonsil hypertrophy (73; 54.1%), nasal septal deviation (3;2.2%) and acute infectious rhinitis (23; 17.1%).

Conclusion: The topical decongestation demand was pretty much less when fixed. Patients with nasal septal deviation and nasopharyngeal tonsil inflammation (56.3%) not needed in TD at all. The topical decongestants usage was acceptable in case of acute infectious and allergic rhinitis but in case of short course of application.

TP1034 | The prevalence of high risk of obstructive sleep apnea in patients with allergic rhinitis

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Background: Allergic rhinitis (AR) is accepted as a risk factor for obstructive sleep apnea (OSA). The prevalence of OSA in patients with AR was reported to be 36%. However, that prevalence in Thai patients is unknown. The relationship between the severity of AR and OSA are undetermined in previous literatures. The objective of this study was to determine the prevalence of high risk OSA in Thai patients with AR as well as the relationship between the severity of AR and OSA.

Method: Patients whose skin prick tests were positive in the ENT allergy clinic, Siriraj Hospital between October 2014 to November 2015 were recruited in this study. They filled in the STOP-Bang questionnaire, the Allergic Rhinitis and its Impact on Asthma (ARIA) classification and visual analog scale for the AR symptoms. High STOP-Bang score indicates a high probability of OSA. The data were collected and analyzed to determine the prevalence of high risk OSA in AR patients as well as the relationship between the severity of AR and the OSA.

Results: One hundred and twenty patients whose skin prick tests positive were included. Twenty-eight patients (23.3%) had high risk of OSA. There was no relationship between the severity of AR and OSA (P = 0.6). However, the duration of AR symptoms was significantly related to the risk of OSA (P = 0.01).

Conclusion: The prevalence of high risk OSA in Thai patients with AR was 23.3%. In patients with AR, careful history of possible OSA and thorough evaluation of the upper airway are essential.

TP1035 | Development and assessment of a novel nasal polyposis symptom diary

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Background: This study collected information on patients' experiences with nasal polyposis (NP) to develop and assess the content validity of a novel NP symptom diary (NPSD).

Method: We developed a novel NPSD based on input from patients who were recruited through physician referral and patient organizations. To evaluate the NPSD, combined concept elicitation and cognitive interviews were conducted with 20 U.S. and 10 U.K. patients who had a physician-verified diagnosis of NP and a history of intranasal corticosteroid use. Patients were asked to discuss their NP symptoms via a series of open-ended questions and follow-up queries. The relative importance of each symptom was characterized by patients using a level of disturbance scale ranging from 0 (not at all disturbing) to 10 (extremely disturbing). Cognitive interviews were conducted to evaluate patients' comprehension of NPSD content and their ability to provide meaningful responses within the specified recall period using the provided response options.

Results: Several prevalent and disturbing symptoms were identified across patient interviews, including nasal congestion (mentioned by 100% of patients; average disturbance rating = 7.9), nasal blockage/obstruction (97% of patients; disturbance = 8.2), difficulty with sense of smell (97% of patients; disturbance = 7.6), facial pressure (90% of patients; disturbance = 6.2), postnasal drip (87% of patients; disturbance = 6.5), runny nose (87% of patients; disturbance = 6.2), facial pain (80% of patients; disturbance = 6.3), and headache (77% of patients; disturbance = 6.5). Saturation was achieved for concepts proximal to NP. The symptoms considered most relevant to NP patients were included in the NPSD, as were items to record NP impact on sleep, daily activities, and patient-reported nasal medication adherence. Cognitive interviewing results indicated that patients understood these items and could select a meaningful response when asked to rate symptom severity or impact at its worst in the past 24 hours using a 4-point response scale (none, mild, moderate, and severe).

Conclusion: Patients attributed multiple symptoms to NP, identifying many as highly disturbing and impactful on sleep and daily activities. Findings from patient interviews support the content validity of the NPSD as a suitable tool for capturing NP symptoms and their impact. Evaluation of the measurement properties of this tool within the context of clinical studies is warranted.

MONDAY, 3 JUNE 2019
TPS 24
EPIDEMIOLOGY OF FOOD ALLERGY II

TP1036 | Prevalence of food hypersensitivity in relation to IgE sensitisation among the general adult population in West Sweden

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Background: The prevalence of self-experienced adverse reactions to foods seems to have an increasing trend in both adults and children. It is unclear if the prevalence of food hypersensitivity in the Swedish adult population is still rising, and which are the most common foods to which adults are more frequently IgE-sensitised.
Method: In a cross-sectional study based on questionnaire responses, interviews and clinical examinations as part of the West Sweden Asthma Study, 1042 subjects from the general population, 17-78 years of age, living in Västra Götaland, Sweden, were included. The subjects reported symptoms for 56 specified foods and blood samples were taken to examine the IgE-sensitisation pattern for 9 common foods.
Results: Approximately 32% of adults reported food hypersensitivity, affecting mostly women and subjects less than 61 years old. The foods most often reported to cause adverse reactions were hazelnut (8.9%), apple (8.4%), milk (7.4%) and kiwi (7.3%). Sixteen per cent were IgE-sensitised to common foods, most often to hazelnut (13.3%), peanut (4.9%) and almond (3.0%), while 5.9% reported symptoms and were IgE-sensitised to the same food, mainly to hazelnut (5.3%).
Conclusion: The prevalence of self-reported food hypersensitivity in West Sweden indicates a rising trend. The correspondence between self-reported symptoms and IgE-sensitisation to foods is generally poor, except for hazelnut and almond which exhibit moderate or fair correlation.

TP1037 | Prevalence of pollen food allergy syndrome and accompanying factors in the eastern black sea region

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Background: There is limited data regarding pollen food allergy syndrome (PFAS) in Turkey. The aim of this study was to investigate the prevalence and clinical characteristics of PFAS in adult pollen allergic rhinitis patients (AR) in the Eastern Black Sea region.
Method: Demographic data, skin prick test results of pollen sensitive patients were evaluated. The questionnaires were applied to the "Life Quality Scale for Rhinitis" and "Pollen Food Syndrome Diagnostic Questionnaire" (Skypala IJ, 2013).
Results: A total of 113 only pollen sensitive AR patients (75 K, 38 E) were included in the study. The mean age was 35.29 ± 11.2 (15-68). 27 (23.8%) of the patients had asthma. 67.3% of AR patients were persistent. The mean RLCI score was 25.71 ± 11.7 (1-60). Seventeen patients (15%) had a history consistent with OAS. Fruits and vegetables in all patients, nuts in 6 patients and legume in 1 patient was the culprit food. PFAS was more common in female (P = 0.05). OAS was found to be significantly higher in birch (21.1%), beech (24.19%, hazelnut (26.9%) tree pollens and weed (27.6%) sensitivity (P = 0.027; P = 0.007; P = 0.001; P = 0.038.) There was no difference RLSS scores and presence of asthma in patients with and without OAS.
Conclusion: In the Eastern Black Sea Region, PFAS was found to be more common in female and patients sensitized to birch, beech, hazelnut and weed but did not have any additional effect on quality of life.

TP1038 | Patterns of sensitization to food allergens among patients with atopic dermatitis from the Eastern Siberia of Russia

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Background: Atopic dermatitis (AD) is a chronic immune-mediated inflammatory skin disease. Food allergy is found to be a risk factor for the development of AD. It is well known about increased risk of food sensitization in patients with atopic dermatitis. Data on food allergies in atopic dermatitis are very few, which determines the relevance of studying this problem. Aim. The aim of our study was to analyze allergen-specific IgE patterns to the most common food allergens in atopic dermatitis.
Method: All individuals were Russians from Krasnoyarsk Territory (Eastern Siberia). In this study a screening analysis of blood serum samples from 91 patients aged from 4 months to 18 years was

performed on microarrays. The mean age of the AD patients was 5.0 ± 0.4 years. Of all patients, 52.7% (48) were female. The average duration of the incidence of atopic dermatitis was 4.0 ± 0.46 years. The total IgE and allergen-specific IgE levels to the most common food allergens were estimated: cow's milk allergens (α-lactoglobulin, β-lactoglobulin, casein and bovine serum albumin), eggs (ovalbumin), cereals (gliadin).

Results: In our research 45.1% (41) infants had elevated total immunoglobulin E (IgE) level. Increased level of specific IgE to food allergens was detected in 81.3% (74) patients. The most significant food allergen was a whole egg (ovalbumin) – 81.1% (60) patients. To a lesser degree, considerable levels of specific IgE were reached in response to gliadin - 68.9% (51), cow milk and its components: α-lactoglobulin – 58.1% (43), β-lactoglobulin – 50.0% (37), casein – 70.3% (52), bovine serum albumin – 62.2% (46). In atopic dermatitis the prevalence of polyvalent sensitization to cow's milk, eggs, gliadin was noted – 31.1% (23), while monovalent sensitization to food allergens was found in 16.2% (12) cases to cow milk and its components – 41.7% (5), ovalbumin – 41.7% (5) and gliadin – 16.6% (2).

Conclusion: Thus, atopic dermatitis as a manifestation of food allergy in children is most often an IgE-mediated disease, which characterized by sensitization to food allergens with a predominance of sensitization to ovalbumin, casein and gliadin.

TP1039 | Prevalence of self reported food allergy in adults at a federal university in Niteroi, Brazil

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Background: In the last decades an increase in Food Allergy (FA) prevalence has been observed. However, there are few studies on FA prevalence in adult population. This project aims at identifying the prevalence of self-reported FA in adults (> 18 years) who work or study at the Fluminense Federal University (UFF) in Niteroi, Brazil.

Method: Cross-sectional epidemiological survey using a standardized questionnaire to assess the prevalence of self-reported FA in adults validated by *Lozoya-Ibanez et al*, 2011 in Portugal. Although it was written in Portuguese (from Portugal), small modifications were introduced for a better understanding in Brazil. The questionnaire was converted to digital format using the Google Forms tools and sent electronically to students, employees and professors from various sectors at UFF (database with 55 000 subscribers) in June 2018. The study was approved by the Committee of Ethics and Research at Hospital Universitário Antônio Pedro.

Results: Six hundred and seventy-three questionnaires were analyzed. Among these, 64.9% were female, 73.4% students, 14.1% teachers, 11.5% administrative technicians, 45.3% have not finished university studies and 23.4% have completed. In addition, 74.4% live in the Metropolitan Region of Rio de Janeiro. Considering the reports of allergic reaction to some food (n = 273), the majority is found in the age group from 20-29 years (42.8%) and the minority with 70 years old or more (0, 37%). The prevalence of self-reported FA was 40.5% (n = 273), predominating reactions to shellfish (40.7%), cow milk and derivatives (37.7%), peanuts (15.8%) and fruits (15.8%). Medical diagnosis of the FA was reported by 60.8% of those who were interviewed and positive family history of allergy by 59.8%. In relation to the foods described as involved in anaphylactic reactions, egg (20%) and beef (14.29%) presented the highest percentage of occurrence. Among the participants who reported allergy to milk and dairy products, abdominal symptoms predominated (69.9%), while in those who reported allergies to shellfish there was a higher incidence of urticaria symptoms (56.7%).

Conclusion: The prevalence of self-reported FA in the study population is clearly overestimated. The high percentage of reactions to shellfish and peanut is consistent with what has been observed in FA studies in adults. The high prevalence of cow milk reactions may be related to symptoms of lactose intolerance, commonly mistaken with FA.

TP1040 | Effects of folic acid supplement intake during pregnancy on food allergy onset in female children

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Background: There are an increasing number of reports on the effects of folic acid intake during pregnancy on the onset of allergies in children. To date, we have reported that folic acid reduces the risk of food allergy onset in high-risk male children whose father or mother had atopic dermatitis or food allergies. In this study, we report the effects of folic acid supplement intake on female children.

Method: Self-administered surveys were distributed to parents during their 18-month checkup in 2013-2015. 7923 respondents were classified into 3 groups based on the level of folic acid intake: those who started taking folic acid within 2 months of pregnancy for a minimum of 4 consecutive months (FOL++), those who took folic acid for any other duration during pregnancy (FOL+), and those who had no folic acid intake (FOL–).

Results: In male children whose mother or father had a history of atopic dermatitis but whose mother had no egg intake during pregnancy, the rate of food allergy onset was 11.6% (n = 43) in the FOL++ group and 36.8% (n = 76) in the FOL– group, similar to our previous results. However, among female children whose parents had similar

allergies, regardless of egg intake, the rates of food allergy onset were 22.2% (n = 180), 13.8% (n = 240), and 13.9% (n = 317) for the FOL++, FOL+, and FOL− groups, respectively, with the FOL++ group having the highest rate. In female children whose mothers' had food allergies in the case of without egg intake, suppression of allergy onset by folic acid was observed. Therefore, the exclusion criteria included children whose mothers had a history of food allergies and low-birth-weight children, as allergy onset was approximately half among low-birth-weight children with no effect by folic acid observed. A logistic analysis was performed between the FOL++ and FOL− groups on the remaining 394 children, with an odd ratio of 2.38 (95% confidence interval, 1.36-4.18) after adjusting for other factors, such as birth order, egg intake, exclusive breastfeeding, and caesarian sections. Therefore, the results suggest that there could be an increased risk of developing food allergies in female children whose mothers had continuous folic acid intake from the first trimester.

Conclusion: The effects of folic acid are considered to vary depending on the gender of the child as well as other factors. Thus, the mother's folic acid intake during pregnancy may have a possible effect on allergy onset in female children as well.

TP1041 | Investigation of culprit foods and symptomatic severity in korean adult food allergy: Single-center experience

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Background: Food allergy (FA) is an emerging public health problem that affects up to 10% of population worldwide. In Korea, changes in dietary habits and the increasing prevalence of allergic diseases are prominent, public concerns for FA is also increasing day by day. Because causative food allergens are quite different between Western and Eastern Asian countries, understanding current clinical features of Korean adult FA is important. The aim of this study was to investigate the culprit allergen and its severity in Korean adult FA patients.

Method: Eight hundred twelve adult patients who suspected as having FA were enrolled. For diagnosis, detailed history taking, ImmunoCAP specific IgE measurement and/or skin prick test, prick to prick test was done.

Results: Among 812 patients, only 415 patients were finally diagnosed as FA. One hundred fifty-five (37.3%) were diagnosed as oral allergy syndrome (OAS), followed by crustaceans (111, 26.7%), wheat (63, 15.1%), fruit allergy without OAS (43, 10.3%), peanut (31, 7.4%), walnut (25, 6.0%), α-Gal allergy (12 patients, 3.6%), silk worm pupa (13, 3.1%). Allergy to egg, milk, fish were rare in adults. One third of the total subjects have multiple allergies to foods (125 of 415, 30.1%), and average number of causative allergens was 2.39. One hundred twenty-nine FA patients (31.0%) had diagnosed as anaphylaxis, and wheat was the most-frequent culprit food in patients with anaphylaxis. Especially, crustacean, wheat, buckwheat, red-meat showed higher proportion of anaphylaxis to total allergy patients. In addition, 20 patients were further diagnosed as food dependent exercise induced anaphylaxis (FDEIA).

Conclusion: Wheat, fruits (apple, peach), crustacean (shrimp, crab) are important allergens in adult FA, which are quite different from food allergen in child. In particular, it was noticeable that proportion of non-classical allergies (OAS, WDEIA, α-Gal allergy) were high in the anaphylactic patients.

TP1042 | Clinical manifestations and outcomes of allergic reaction to shellfish in adult and children: Data from the food allergy research & education (FARE) registry

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Background: Shellfish is one of the most common food allergens. We reviewed the clinical outcomes of allergic reaction to shellfish.

Method: Patient-reported data on shellfish allergy in the FARE registry (May 2017 to August 2018) were analyzed.

Results: Of the 5547 participants, 531 reported having shellfish allergy; 63 of these completed a questionnaire on allergic reactions, and 44/63 had sufficient data for analysis (27 children under 18 years, 17 adults). Shrimp was the most common shellfish allergen (59% children, 82% adults), followed by crab and lobster. Thirteen patients (30%; 7 children, 6 adults) described their reactions as severe. In children, skin manifestations were more common than gastrointestinal (GI) (82% and 74%, respectively), while in adults GI manifestations were more common than skin (82% and 71%, respectively). Seventy-two percent of reactions occurred within 10 minutes (78% children, 63% adults) and 73% occurred following exposure by ingestion (71% children, 77% adults). The remainder were cutaneous and inhalation exposures. Epinephrine injections were administered in 7 patients (16%); one child and 2 adults required the second dose. Biphasic reactions occurred in 9 patients (20%; 5 children and 4 adults) and mostly between 1-5 hours after exposure (56%; 1 child and 4 adults). One child (4%) and 3 adults (18%) required hospitalization for management of reactions.

Conclusion: The most common reported allergic reactions to shellfish in children and adults were skin and GI manifestations. Symptom onset, epinephrine use, and the incidence of biphasic reactions were

similar between children and adults. Despite some epinephrine use, a few patients required hospitalization.

TP1043 | The most precious milk

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Background: Exclusively breast-fed babies are brought to the allergist, experiencing digestive reactions, even if the mother has a healthy and nutritionally balanced diet. The most common digestive reactions in infants, where the infectious factor has been excluded, are reactions to foods. These may be IgE or non-IgE mediated. Non-IgE mediated food allergies include a large number of gastrointestinal disorders (celiac disease, food protein induced enterocolitis syndrome (FPIES), allergic proctocolitis (AP), proteins induced enteropathy (FPE), cow's milk induced anemia), cutaneous disorders or lung disorders.

Method: Prospective study on a group of 7 patients aged 6 months and younger, exclusively breast-fed, who were brought to the allergy service during four months (August-November 2018) due to repeated stool changes: blood stains, streaks or blood mixed with mucus, otherwise healthy children, with a normal growth curve. Inclusion criteria: laboratory confirmation of blood in the stool of patients up to 6 months old, excluding digestive infections. Exclusion criteria: lack of laboratory confirmation of the presence of blood in the stool, or/and to which the infectious factor could not be excluded.

Results: Of 7 children, in 6 was confirmed the presence of blood in stool, and in these cases mothers were advised to keep a rotation diet, ruling out the main foods incriminated in studies, to be the cause of allergic proctocolitis. Each of these, at a time, was not consumed for 10 days: The cow's milk and dairy products, eggs, wheat, apple and carrot. The mothers kept a food diary and noted the appearance of the stool, in parallel. Four out of six children responded positively by disappearance of symptoms, excluding milk from mother's diet, a child reacted positively to exclusion of egg from the mother's diet. One child had only amelioration (decrease frequency of bloody stools) to the exclusion of milk and then apple, from the mother's diet, but their exclusion further together did not lead to the complete remission of the symptoms.

Conclusion: Cow's milk is rightful blamed for being one of the main allergens in both IgE and non-IgE mediated allergies. Allergic proctocolitis is a clinical entity that is more and more common in clinical practice, the main treatment is the exclusion of the triggering food. When it comes to exclusively breastfed babies, the mother is the one who will keep the diet, due to the passage of ingested food proteins into breast milk.

TP1044 | Persistent and late onset milk allergy: A retrospective study

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Background: IgE mediated cow's milk protein (CMP) allergy is common in infants. Although the allergy resolves in the majority of children, a minority continue to be allergic into adolescence and/or adulthood. Occasionally adult onset milk allergy has been reported.

Method: We retrospectively analysed the demographics, presentation, investigation and management of patients over 12 years of age in allergy clinic with a clinical history of persistent or late onset IgE mediated CMP allergy and a supporting positive skin prick test (SPT), specific IgE to milk and/or challenge to CMP.

Results: 34 patients were included (Males 20, Females 14). The mean age was 23 years (range 12-56). Mean SPT to milk was 6.4 mm (range 0-20 mm) (n = 31/34), mean specific IgE to milk was 28.2 (range 0.06-100 kUA/l) (n = 24/34), mean specific IgE to casein was 20.4 (range 0.02-92.4 kUA/l) (n = 21/34) and the mean specific IgE to whey was 13.02 (range 0.02-48.1 kUA/l) (n = 13/34). Total mean IgE was elevated 2452 IU/mL (range 24-10505) (n = 24/34). Only 15% of the cohort had developed milk allergy in adulthood (n = 5/33). Commonest associated food allergies were egg 84% (n = 27/32), primary nut 53% (n = 17/32), oral allergy syndrome to fruits/nuts 50% (n = 16/32) and wheat 22% (n = 7/32). Regarding atopy, 94% had asthma (n = 29/31), 94% rhinitis (n = 29/31) and 97% eczema (n = 30/31). A significant number of patients avoided any attempt at milk reintroduction 31%(n = 10/32) of those that reintroduced it 36% failed a baked milk challenge (n = 8/22); however, 36% tolerated baked milk on steps 1,2 or 3 of milk ladder (n = 8/22), 14% achieved step 9 or 10 (3/22) and 14% had documented resolution of milk allergy (n = 3/22).

Conclusion: The majority of patients had persistent milk allergy from childhood. Late onset milk allergy was uncommon. Nearly all patients had eczema, rhinitis, asthma and an elevated total IgE. The majority of patients had associated egg allergy. Half of patients had primary nut allergy and pollen food allergy. A significant number (31%) avoided any attempt at reintroduction, of those that did attempt the milk reintroduction 1 in 3 failed a baked milk challenge. However, 2 in 3 patients managed to progress to baked milk or higher on the milk ladder. The resolution of milk allergy occurred in a minority.

TP1046 | General knowledge of food allergy and application of the FIC regulation in bakeries in the Epinal area, France

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Background: Food allergy (FA) is classified as a World Health Issue and its prevalence is increasing quickly. The eviction of the allergen is the first treatment of FA. The mandatory labelling of allergen in non pre-packed food has been ruled by the European Food Information to Consumers (FIC) Regulation since 2015. In France, there are about 38 000 bakeries. Our goal is to assess the knowledge of FA and the application of the FIC Regulation by the employees of the bakeries in the area of the city of Epinal, Vosges, France.

Method: An eighteen-question survey, inspired by a survey used in a similar study in restoration in two French cities, were distributed in 62 bakeries in 26 towns around Epinal. All employees of the establishments were invited to answer the survey anonymously

Results: Forty-nine establishments responded to the survey (5 refusals and 8 didn't reply despite numerous reminders), which represents a 79% response rate. We obtained 52 responses from the bakers, 40 from the salespersons and 10 apprentices. The responses about the general knowledge of FA are correct. Among the 102 respondents, a third know the FIC Regulation and 88% (N = 75) assure that their establishment is following the regulation on the labelling of non pre-packed products. Half of them do it properly. A third of the respondents are interested in a formation in FA.

Conclusion: General knowledge of FA in the bakeries in the area of Epinal, Vosges, France, is satisfying. However, the knowledge and the application of the FIC Regulation are insufficient.

TP1047 | Food allergy sensitization by immunoCAP in Mexican allergic patients

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Background: The prevalence of food allergy has increased over the past decades. Sensitization profiles vary among regions, partly depending on the most frequent staple foods. No large data recollection on *in vitro* IgE sensitization profiles of Mexican allergic patients has been published till now. Food allergy panels are often based on international data.

Method: In a transversal, observational, descriptive and retrospective trial we analyzed ImmunoCAP data from patients of all ages with suspected clinical allergy. All data on sIgE to individual foods, recollected from January 2016-April 2018 were included. Some patients were tested with the full panel (36 extracts), some with only one extract. An age-group comparison was made.

Results: A total of 1795 subjects fulfilled inclusion criteria. The 15 foods most frequently positive (>0.35 kUA/L) were (number of tests/%positive): Hazelnut (63/49.2%), apple (52/32.7%), shrimp (154/26%), peanut (219/24.7%), egg-white (123/23.6%), yolk (52/21.2%) peach (134/19.4%), almond (65/18.5%), tomato (79/17.7%), bean (127/17.3%), milk (1097/16.9%), strawberry (51/15.7%), kiwi (86/15.1%), corn (61/13.1%), wheat (517/13%).

Positivity for some foods was most frequent across different age groups, in children under 5 years: milk ($P = 0.0001$); in older children (6-17 years): peanut ($P = 0.007$), almond ($P = 0.04$), kiwi ($P = 0.003$), wheat ($P = 0.0001$) soy ($P = 0.0001$), corn ($P = 0.05$) and shrimp ($P = 0.03$); in adults: apple ($P = 0.01$).

The following foods had less than 50 samples, but high-positivity (>0.71 kUA/L): rye 60%, mango 42.9%, carrot 37.5%, cashew 27.3%, banana 21.1%, oat 20.6%, melon 15.6% and avocado 15.2%.

Conclusion: We suggest food allergy panels recommended for Mexicans should include hazelnut, beans and corn. These are not often tested and with the data obtained, seem of importance. Rye, mango, carrot, chestnut, banana, oat, cantaloupe and avocado allergy prevalence should be investigated further. A large prospective trial should validate our data.

TP1048 | Sesame seed allergy—Same food, different allergens?

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Background: Sesame seeds (SS) have been increasingly incorporated in various food items, with a consequent augmented risk of hypersensitivity reactions, often severe. Despite this, few case reports have been published in Europe. So far, 7 sesame seed allergens have been identified (Ses i 1 to Ses i 7). The authors describe a series of 5 patients.

Method: Retrospective study of patients with SS allergy (SSA) from 2012 to 2018. The diagnosis of SSA was based on a clear medical history and positive skin prick tests (SPT) and/or positive specific IgE for SS. Collected data were age, gender, clinical symptoms, result of diagnostic tests, presence of sensibilization and/or cross-reactivity with other seeds or nuts.

Results: 5 patients (3 females), mean age 31 years (range, 4-46 years) were included, as described in table 1. Anaphylaxis occurred in 4 patients, oral allergy syndrome in 1. Three patients had SS exposure at workplace or hobby. Ses i 1 specific IgE (ImmunoCap ISAC) was positive in 3 patients. Two patients had asymptomatic sensitization to other tree nuts or others seeds and 2 reported symptoms to other seeds and nuts. One was monosensibilizated to SS (no symptoms

CASE	Age	Gender	Suspect Food	Reaction	SPT SS	Sesame IgE (UK/l)	nSes i1 (ISAC)	SPT Others Seeds/ nuts	ISAC Others Seeds/Nuts	Clinical allergies
1	45	Female	Bread	Oral allergy syndrome	+ (3 mm)	ND	0.4	Pumpkin Sunflower Almond Cashew Hazelnut Pistachio Walnut	Ana o 2 Cor a 9 Gly m 6	Almond, Chickpeas Hazelnut Walnut
2	15	Male	Hamburger bun	Anaphylaxis	+ (9 mm)	0.55	-	Pumpkin Sunflower Hazelnut Peanut Walnut	nsLTPs Ara h 9 Cor a 8 Jug r 3 Pru p 3	-
3	4	Male	Bread sticks	Anaphylaxis	+ (10 mm)	2.55	-	-	-	-
4	44	Female	Hamburger bun	Anaphylaxis	+ (10 mm)	ND	16	Sunflower	Cor a 9	Sunflower Flaxseed, Walnut
5	46	Female	Sesame seeds snack	Anaphylaxis	+ (15 mm)	2.60	0.4	Sunflower	-	-

– = negative; + = positive; ND = not determined

or positive tests to other seeds or nuts). Ses 1 was negative in 2 patients. In 1 patient, the only identified allergens were non-specific Lipid Transfer Proteins (nsLTPs). Two patients were sensitized to storage proteins.

Conclusion: SSA occured at all ages, including 1 child. The majority of reactions were severe. Patients presented different patterns of SSA, with diverse implicated allergens and cross-reactivities. Although nsLTPs have not been previously identified in SS, in 1 patient it was the only identified allergen. SDS-PAGE and inhibition assays will be useful to better characterize SSA patients

TP1049 | Anaphylactic reaction to paprika: A case series in a child and adult patient without prior risk factors

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Case Report:

Introduction: Paprika is a common spice that is used worldwide in a variety of dishes and pre-packaged foods. It is made by grinding dried forms of chilli peppers belonging to the *Capsicum annuum* species. Cases of allergies to paprika are extremely rare and occurs almost exclusively in adults and those with sensitization to mugwort or birch, as part of a mugwort-birch-celery-spice syndrome. We present a rare case of paprika associated angioedema in a child and an anaphylactic reaction in a woman with no prior occupational exposures, pollen allergies, or other known risk factors.

Methods: Skin prick testing (SPT) and serum specific IgE were performed to confirm an anaphylactic type reaction to paprika.

Case 1: A 5-year-old boy presented with an episode of acute angioedema involving his oral mucosa after eating a popular prepackaged tortilla chip snack and recurrent episodes after cracker snacks. Reactions were immediate in both cases with no associated urticaria, nausea, or vomiting.

SPT to Doritos chips, Goldfish crackers, and common foods was performed. Test was remarkable for 8 mm Doritos chips and 8 mm Goldfish crackers, with a positive histamine control of 5 mm.

Paprika was found to be a common ingredient of Doritos chips and Goldfish crackers. He underwent further SPT testing which revealed a positive reaction to paprika extract (10 mm), cayenne pepper (10 mm), and chilli pepper (6 mm), with a 4 mm histamine control. His serum specific IgE was measured to be positive to paprika (51.0 kU/L).

Case 2: A 47-year-old woman presented for evaluation after experiencing an acute reaction to a chick pea and paprika dish. She described throat tightness, generalized pruritus, nausea, vomiting, and abdominal cramping. She was otherwise in good health, with no history of allergic rhinitis.

SPT to paprika extract, chick peas, common foods, and inhalants was remarkable for 5 mm dust mite and 6 mm paprika, with a 4 mm histamine control. She tested negative to chick pea. Serum specific IgE results to paprika and chick pea were requested.

It was determined that her anaphylactic reaction was secondary to paprika.

Conclusion: Paprika remains a widely used spice with only rare cases of described allergy. We described two unique cases of severe allergic reactions to paprika in patients with no known history of risk factors. Although reactions to paprika are rare, they must be considered when investigating both children and adults with allergic reactions to food containing spices.

TP1051 | Poppy seed allergy in the Czech Republic

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Case report: Poppy seed allergy is rare, but its manifestation is usually severe with immediate IgE- mediated reaction. Symptoms may include urticaria, angioedema, dyspnoea and anaphylaxis. Specific IgE and skin prick testing (prick-to-prick) is available. Co-sensitisation with other seeds, nuts, and buckwheat has been described.

Seeds of a plant Papaver somniferum are traditionally used in the Czech cuisine mainly for toppings in sweet dishes or fillings in sweet pastries. They are also used at bakeries as sprinkled garnish over rolls and buns. Homemade breadcrumbs (grinded old pastry) may cause reactions in very sensitive individuals due to trace amounts of poppy seeds. Therefore, thorough review of patient history may uncover this allergen where it would be easily overlooked.

A small patient cohort from our paediatric allergy department with poppy seed allergy and reactions ranging from urticaria to anaphylaxis is presented to highlight this often-overlooked allergen. Our local practice includes routinely testing for presence of poppy seed allergy in suspected food allergy cases without clear culprit trigger because of its almost ubiquitous presence in pastry.

TP1052 | The global incidence and prevalence of anaphylaxis in children in the general population: A systematic review

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Background: Despite an increasing number of publications from individual countries and regions, there is still no systematic review of the global epidemiology of anaphylaxis in the general paediatric population.

Method: We conducted a systematic review, using a protocol registered and published with the international prospective register of systematic reviews (PROSPERO). Results were reported following PRISMA guidelines. The search strategy was designed in Medline (ovid) and modified for Embase (ovid) and PubMed. Papers were screened by two independent reviewers following selection and exclusion criteria. Data extraction and risk of bias assessment were completed by the same two reviewers. Studies in adults only or those that did not report data in children separately were excluded.

Results: A final total of 59 articles were included. Of these, 5 reported cumulative incidence, 39 reported incidence rate and 17 reported prevalence data. The incidence of anaphylaxis in children worldwide varied widely, ranging from 1 to 761 per 100 000 person-years for total anaphylaxis and 1 to 77 per 100 000 person-years for food-induced anaphylaxis. The definition of anaphylaxis from NIAID/FAAN was the most commonly used. Gender and ethnicity were demographic risk factors associated with anaphylaxis in children. Increasing total or food-induced anaphylaxis incidence over time were reported by 19 studies.

Conclusion: The reported incidence of anaphylaxis in children varied widely. Studies in developing countries are underrepresented. To accurately compare anaphylaxis incidence between countries and investigate the time trends, further studies using a standardised definition across different countries are required.

TP1053 | Food-induced anaphylaxis among infants and children up to 2 years of age

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Background: The incidence of food-induced anaphylaxis is observed to be still increasing among infants and small children. The clinical presentation often causes diagnostic and therapeutic difficulties in this age group.

The objective of the study was to characterize the symptoms and the management of the food-related anaphylaxis among infants and small children up to 2 years of age.

Method: A retrospective study included 68 children (39 boys, 57%) up to 2 years of age (mean age 13.3 ± 5.7 months; median 10.5 months) hospitalized in the Department of Pulmonology and Allergy between 2014 and 2018.

Symptom severity was assessed according to Sampson's et al grading for food-induced anaphylaxis. We also looked for cofactors that increased the risk of severe anaphylaxis.

Results: The cow's milk (CM; n = 34, 50%) and egg (n = 23, 34%) were the most common food allergens implicating anaphylaxis. The average time from contact with an allergen to the occurrence of symptoms was 14 minutes (median 10 minutes). The most common manifestations were: urticaria (88%), face angioedema (68%) and vomiting (51%). A cough was the most frequently reported symptom of the respiratory system (50%). Severe symptoms of anaphylaxis occurred in case of 24 children (35%), out of which only two patients

(8%) received adrenaline intramuscularly. The severity of the allergic reaction correlated with egg allergy and presence of asthma as a concomitant disease. The symptom most common reported by parents of children with severe anaphylaxis was – as they described it - the "floppy child" (n = 16, 67%). The treatment was initiated by parents in 70% of children at home and involved administration of an antihistamine and /or calcium preparation. As part of Emergency Team intervention the antihistamines (84%) and systemic corticosteroids (72%) were mainly used.

Conclusion: Assessing the severity of food-related anaphylaxis among very young children may pose diagnostic and therapeutic difficulties. Asthma and egg allergy were the risk factors of anaphylaxis severity. In the initial treatment of anaphylaxis in the Emergency Department was based on the administration of antihistamines and corticosteroids. Adrenaline as a first-line treatment was used sporadically.

TP1054 | Peanut induced anaphylaxis in children and adolescents: Data from the European anaphylaxis registry

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Background: Peanut allergy has a rising prevalence in high-income countries, affecting 0.5-1.4% of children, and is one of the most common cause of severe and fatal allergic reactions related to food. This study aimed to provide data on peanut anaphylaxis in European children and adolescents, with regards to symptoms timing and severity, previous reactions, co-factors, emergency and long-term management.

Method: Data were sourced from the European Anaphylaxis Registry, collected from 10 European countries via an online questionnaire, after in-depth review of cases with peanut anaphylaxis in a tertiary paediatric allergy centre.

Results: Anaphylaxis due to peanut was recorded in 459 patients younger than 18 years (median age 5 years) between July 2007 and March 2018, representing 85% of all registered cases of peanut anaphylaxis. Respiratory (423; 92%) and skin (418; 91%) symptoms were predominant, with the majority of cases (304; 66%) labelled as severe anaphylaxis (grade III-IV according to Ring-Messner classification). Reactions occurred within 10 minutes of exposure in 49% (226) of cases. 42% of patients experienced previous reactions to peanut, usually milder. 114 (25%) cases reported relevant co-factors, with physical exercise (91; 80%) and infection (16; 14%) being the most frequent. 110 (24%) cases were solely lay treated, professional treatment was mainly carried out by emergency physicians (119 out of 306 cases; 39%). Intramuscular adrenaline was administered as first line treatment in only 39% of cases, including self-administration in 15%, and professional administration in 24%. 170 (62%) of 276 cases with known hospitalisation status required admission, only 6% to Intensive Care Unit. There were 3 cases of fatal anaphylaxis. 97% of cases received counselling about trigger avoidance, prescription and training in using emergency drugs as part of long-term management.

Conclusion: The European Anaphylaxis Registry data confirmed peanut as one of the major causes of severe allergic reactions in children. Usage of intramuscular adrenaline as first line treatment is low and needs to be improved. The Registry, designed as the largest database on anaphylaxis and working towards observing trends over time, allows continuous assessment of this condition.

MONDAY, 3 JUNE 2019
TPS 25
IMPACT AND MECHANISM AT THE RESPIRATORY BARRIER

TP1056 | Long-term intranasal exposure to house dust mite allergen in mice without systemic sensitization leads airway remodeling

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Background: Asthma is a chronic respiratory disorder characterized by bronchial hyperreactivity and airflow obstruction, which is induced by chronic airway inflammation. Repeated exposure of allergens into respiratory tract cause the chronic inflammation, leading to damage lung cells and tissues followed by structural change. Airway remodeling, which is one of the features observed in chronic stage of allergen-induced airway inflammation. In this study, we aimed to determine whether airway remodeling could be developed in the murine experimental model by long-term intranasal exposure of house dust mite(HDM) allergen without inducing systemic sensitization.

Method: BALB/C mice were intranasally instilled with HDM extract (*Dermatophagoides pteronissunus*) for three times a week for 8 consecutive weeks. Airway allergic inflammation including cytokine secretion, immune cell recruitment, and mucus production were assessed. Also, airway remodeling such as the deposition of collagen and fibronectin, and goblet cell hyperplasia were performed.

Results: Long-term intranasal exposure to HDM allergen resulted in elevated inflammatory cytokine levels and neutrophil recruitment in BALF, as well as IgE level in plasma. The increased deposition of collagen and fibronectin, as well as goblet cell hyperplasia, were observed in lung tissue of long-term intranasal exposure HDM allergen. And the levels of soluble collagen, TGF-ß, and laminin were elevated in lung and plasma. These findings showed that long-term HDM intranasal administration without inducing systemic sensitization in a murine model promoted chronic inflammation and airway remodeling.

Conclusion: This murine model based on long-term intranasal administration without inducing systemic sensitization showed that the induction of chronic inflammation and airway remodeling was associated with exposure to HDM allergen. These features suggest that this model could be useful experimental model for the researches, as a model mimicking chronic allergen exposure in human.

TP1057 | Safety, tolerability, pharmacokinetics and pharmacodynamics of AUR101, An RORγt inhibitor, in normal healthy volunteers

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Background: Th17 are a type of helper T cells which produce IL-17 in response to antigen recognition. Th17 differentiation and consequent production of IL-17 is dependent upon the transcription factor RORγt. Studies have suggested causative involvement of Th17 cytokines in various autoimmune diseases such as psoriasis. RORγt is therefore an attractive target for pharmaceutical intervention. Clinical validation of this pathway comes from the therapeutic efficacy of IL-17 antibodies, such as secukinumab, in several autoimmune disorders. AUR101 is an oral inhibitor of RORγt and has shown efficacy in imiquimod as well as IL-23 induced psoriasis models.

Method: INDUS is an ongoing Phase I study of AUR101 in healthy volunteers. The primary objective is safety/tolerability and the secondary objectives include PK, food-effect and PD evaluation in an *ex vivo* whole blood-based IL-17A secretion assay. The study is designed in Single Ascending Dose (SAD) and Multiple Ascending Dose (MAD) fashion. A Safety Review Committee (SRC) reviews data before dose escalation.

Results: As of January 13, 2019, 39 healthy subjects across four cohorts of SAD and one cohort of MAD have been dosed with AUR101/matching placebo. The maximum AUR101 dose administered in SAD cohorts is 600 mg, and MAD cohort 1 subjects have received AUR101/matching placebo at 500 mg QD x 14 days. No serious adverse events or any safety signals have been observed. Non-serious AEs have been as expected in a healthy volunteer population, without any concern. The laboratory parameters have almost universally been normal with a few deviations considered as clinically non-significant. Specifically, all liver function tests and kidney function tests have been in the normal range. The Day 14 PK in MAD Cohort 1 is ~ 5-6 times lower than NOAEL dose exposures in 90-day toxicology studies in rats and dogs and the elimination half-life is calculated as approximately 14 hours. In the *ex vivo* whole blood assay of IL-17A secretion, five (5) out of six (6) participants receiving AUR101, showed ~ 80% or more reductions from the pre-dose baseline. Additional MAD cohorts are being planned.

Conclusion: At exposures that are multiple folds lower than preclinical NOAEL dose exposures in rats and dogs, AUR101 is showing

excellent and promising PD (RORγt dependent IL-17) modulation in healthy volunteers without any clinical concerns. Updated safety and PK/PD data will be presented at the meeting.

TP1059 | Immunomodulatory effects of PON1 on airway inflammation and remodeling in bronchial asthma

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Background: The nanosized vesicles secreted from the various cell types into the surrounding extracellular space are called extracellular vesicles (EVs). Although stem cell-derived extracellular vesicles (EVs) are known to promote regeneration of damaged tissues, there is no report evaluating immune modulating effects of stem cell-derived EVs, particularly Paraoxonase-1 (PON1) on Th2 mediated inflammation. This study aims to evaluate the immunomodulatory effects of PON1 on Th2-mediated inflammation.

Method: C57BL/6 mice were sensitized to OVA using intraperitoneal injection and intranasal challenged with OVA. To evaluate the effect of PON1 on allergic airway disease, 10 μg/50 μl of control supernatant, ASCs supernatant with PON1 were administrated both intraperitoneally and intranasally before OVA challenge. HE, PAS and Giemsa staining stains were used to evaluate airway inflammation and inflammatory cells in bronchoalveolar lavage fluid (BALF). qRT-PCR and Western blot and ELISA were used to detect PON1 expression, inflammatory cytokines and immunoglobulin, and colorimetry was used to detect PON1 activities. We evaluated airway hyperresponsiveness (AHR), cytokine profile of bronchoalveolar lavage fluid (BALF) and lung draining lymph nodes (LLN) and lung histology.

Results: PON1 significantly inhibited eosinophilic inflammation in the lung. AHR, total inflammatory cells and eosinophils in BALF were significantly decreased in both intraperitoneal and intranasal administration of PON1. Furthermore PON1 significantly inhibited Th2 cytokines (IL-4 and IL-13) in the LLN and IL-4 in BALF and significantly enhanced regulatory cytokines (IL-10 and TGF-beta) and IFN-γ in the BALF.

Conclusion: PON1 could inhibit the secretion of LPS-induced macrophage inflammatory cytokines and the proliferation of lung fibroblasts and ameliorate allergic airway inflammation in asthmatic mice.

TP1060 | The expression level of proinflammatory cytokines depending on the difference of microbiome among mites; dermatophagoides farinae, dermatophagoides pteronyssinus and tyrophagus putrescentiae

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Background: House dust mites and storage mites are well-known allergen source to induce allergic disease. In addition to allergens, the endotoxin and bacterial DNA, adjuvants of allergen, are derived from the microbiota in the mites. Allergens and endotoxin stimulate cells to secrete the pro-inflammatory cytokines and chemokines to induce immune response. Recently, it was revealed that the microbiome of mites grown on the same condition was different according to the species. However, it was not known whether the difference affects to expression level of pro-inflammatory cytokine and chemokine from human bronchial epithelial cell.

Method: Three species of mites (*D. farinae*, *D. pteronyssinus*, and *T. putrescentiae*), major allergens to cause allergic disease, were cultured in same conditions (autoclaved media, 80%RH, 25°C) and microbiome of each species was analyzed by using the next generation sequencing. We measured the level of major allergen of *D. farinae* and *D. pteronyssinus* and the level of endotoxin of three species of mites. We cultured BEAS 2B cell, human bronchial epithelial cell line, and treated the protein extract (100 μg/mL) of three species of mites to measure the expression level of pro-inflammatory cytokine and chemokine, IL-6 and IL-8.

Results: The major allergens of *D. fariane* (Der f1 and Der f2) were less than those of *D. pteronyssinus* (Der p1 and Der p2). In *D. farinae* and *T. putrescentiae* were composed to mostly gram-negative bacteria. In *D. pteronyssinus* grown on the autoclaved medium, only a few bacteria were seen in contrast to the other two species. Corresponding to the result of microbiome, the endotoxin levels of *D. farinae* and *T. putrescentiae* were much higher than that of *D. pteronyssinus*. The IL-6 and IL-8 level from BEAS 2B cell treated with extracts of each species were comparable to each other.

Conclusion: The microbiota composition of mites affects to the level of endotoxin. Allergens and endotoxin, adjuvants, affect the expression level of pro-inflammatory cytokine and chemokine from human bronchial epithelial cell in cooperation. However, the detailed mechanism is not known well and it is needed to study further.

TP1061 | Damage-associated molecular patterns molecules as a possible biomarker in allergic airway inflammation

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Background: Various inflammatory mediators have been found to be involved in the pathogenesis of allergic disease (AR). The role of heat shock proteins in AR has not been studied. The aim of this study was to investigate the levels of heat shock protein 70 (Hsp70) in the nasal lavage fluids of AR patients and controls to elucidate the role of Hsp70 in the pathogenesis of AR.

Method: Using an enzyme-linked immunosorbent assay, the levels of Hsp70, Hsp90, HMGB1, interleukin (IL)-4, IL-13, and IL-8 in nasal lavage fluid from patients were measured and statistically analyzed. Primary human nasal epithelial cells were cultured in vitro and T-helper 2 (Th2) cytokines (IL-4, IL-13) were added to the culture medium. We evaluated the mRNA and protein expression levels of Hsp70 using realtime polymerase chain reaction and western blot assay.

Results: Hsp70 was easily detected in nasal lavage fluid and the levels of Hsp70 were higher in AR patients than in healthy controls. Other clinical characteristics of subjects were not significantly associated with Hsp70 levels. Furthermore, we found that treatment with IL-4 and IL-13 induced the secretion of Hsp70 in human nasal epithelial cells.

Conclusion: We found that Hsp70 was abundant and positively detected in nasal lavage fluid samples from all subjects, and that Hsp70 levels were significantly higher in AR patients. We demonstrated, both in vivo and in vitro, that Hsp70 could play an important role in the pathogenesis of AR, and we suggest that Hsp70 can be used as a disease marker for AR.

TP1062 | Effect of intermittent hypoxia from obstructive sleep apnea on respiratory allergic disease

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Background: Patients with sleep apnea frequently present with nasal symptoms. To date, these symptoms have been thought to be indirect consequences of physical airway obstruction and mouth breathing. However, clinical studies have recently been reported that intermittent hypoxia, which of main pathophysiology of sleep apnea, directly causes inflammation and also affects allergic symptoms. Therefore, we hypothesized that sleep apnea affects respiratory immune system, affecting inflammation and allergic diseases. We studied how the immune processes lead to these results.

Method: First, we constructed sleep apnea mouse model that effectively represents sleep apnea. Next, in the process of producing the allergic rhinitis mouse model, the presence of intermittent hypoxic conditions, whether there were any allergic nasal symptoms or allergic related molecules, was examined. A total of 20 BALB/C mice were used. Each group was divided into 10 control groups: allergic rhinitis mouse model expression with ovalbumin and 4 weeks of normal air application, and comparison group: allergic rhinitis mouse model expression with ovalbumin and intermittent hypoxic 4 week application.

Results: After 4 weeks of sleep apnea mouse model construction process, blood and tissue samples were obtained. In mice exposed to sleep apnea, decrease of regulatory T cells among the various immune cells was most characteristic. The allergic rhinitis mouse model was constructed through a four-week course. In the case of mice exposed to intermittent hypoxia, an increase in serum ovalbumin specific IgE was the most characteristic with an increase in the frequency of allergic symptoms including nose scratching. A decrease in regulatory T cells was also observed in this group.

Conclusion: We observed that intermittent hypoxic conditions, which of main pathophysiology of sleep apnea, reduced regulatory T cells in mice and that intermittent hypoxic conditions could enhance allergic expression of allergic rhinitis mice. Thus, we concluded that sleep apnea can affect allergic symptoms in a direct way.

TP1063 | Clinical manifestations and upper respiratory tract microflora composition in patients with primary immunodeficiency in samara region

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Background: Primary immunodeficiencies (PIDs) are rare, genetically determined diseases that cause dysfunctional immunity, clinically presenting mostly as susceptibility to infection. The analysis of microflora composition provides us with required data for adjusting rational complex therapy of these conditions. The purpose of the study was to describe and analyze the distribution and clinical features of PID in Samara region and to determine quantitative and qualitative composition of upper respiratory tract microflora in PID's patients.

Method: Observational study of a cases series. 29 patients aged 3 to 55 years old diagnosed with PIDs from the registry of the Samara Referral Centre for PIDs were analyzed, clinical and anamnestic features of diseases were evaluated. We also examined microflora of

34 loci from upper respiratory tract of 7 patients using MALDI-ToF mass-spectrometry

Results: The male-to-female ratio was 2,2. The median age at the onset of symptoms was 18 months and at the time of diagnosis 11 years. Predominant antibody deficiency diseases take the first place in the structure of PID (62.1%). The consanguinity rate was found only in 10% of families. Recurrent infections, particularly lower airway infections (67 %), presented the most common initial manifestation of PID patients. The lag in growth and physical development was revealed in 54% of patients, repeated deep abscesses of the skin and internal organs, as well as two or more episodes of severe generalized infection - in 46% of patients. Frequent otitis, sinusitis and thrush occurred in only 31% of cases, two or more pneumonias a year - in 28% of patients. Lymphadenopathy was detected in 62% of patients, hepatosplenomegaly in 59% of patients, anemia in 52% of patients and instability of stool in 39% of patients. The results of a bacteriological study of 238 samples of upper respiratory tract mucosa has been analyzed. All examined patients, except for the woman with common variable immunodeficiency (CVID), had dysbiotic states of various degrees of severity, which were characterized with detection of clinically relevant microflora in unusual loci and with the decrease of normobiota's titers.

Conclusion: Patients with PIDs in Samara region had the same age and gender distribution observed in international studies. The study revealed a significant delay in diagnosis (mean 9.6 years) and severe violations in upper respiratory tract microflora composition in PIDs patients.

TP1064 | Extracellular vesicle of adipose-derived stem cells: A role for allergic airway inflammation in asthmatic murine model

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Background: Extracellular vesicles (EVs) are nanosized membranous vesicles, secreted from a variety of cell types into their surrounding extracellular space. Various EVs containing proteins, nucleic acids, and lipid are transferred to recipient cells and affect their function and activity. Several studies have showed that EVs released from inflammatory and epithelial cells implicated allergic disease. However, the role for EVs of adipose-derived stem cells (ASCs) in allergic airway diseases remains unclear. In this study, we evaluated the effects of EVs derived from ASCs on allergic airway inflammation in ovalbumin (OVA) induced asthmatic mouse model.

Method: C57BL/6 mice were sensitized to OVA by intraperitoneal injection and challenged intranasally with OVA. To evaluate the effect of EVs derived from ASCs on allergic airway disease, 10 μg/50 μl of control supernatant, ASCs supernatant with or without EV were administrated intranasally before OVA challenge. We evaluated airway hyperresponsiveness (AHR), the proportion of eosinophils in bronchoalveolar lavage fluid (BALF), lung histology, serum total and OVA-specific antibody, cytokine profile of BALF and lung draining lymph nodes (LLN), and T cell population of LLN.

Results: ASCs supernatant with EV significantly inhibited eosinophilic inflammation in the lung. AHR, total inflammatory cells and eosinophils in the BALF were significantly reduced after ASCs supernatant with EV administration. EVs of ASC supernatant significantly decreased the serum total and allergen-specific IgE and total IgG1 level. EVs of ASC supernatant significantly inhibited IL-4 and IL-13 in the LLN and IL-4 in BALF. EVs of ASC supernatant significantly enhanced IL-10, TGF- β and IFN-γ in the BALF. In addition, CD25 + Foxp3 + and IL-10 + T cells in LLN were significantly increased after EVs of ASCs administration.

Conclusion: EVs of ASCs ameliorated allergic airway inflammation and improved lung function through the induction of Tregs expansion. EVs of ASCs may be a regulator for allergic airway disease.

TP1065 | Immune and endocrine parameters of infants with thymomegaly associated with acute obstructive bronchitis

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Background: Study objective: Comparing Immune and endocrine function among 41 infants with radiologically detectable Thymomegaly and 29 infants with no Thymomegaly. All 70 infants at the ages from 6 to 36 months were hospitalized for acute obstructive bronchitis.

Method: Measuring CD lymphocytes, immunoglobulins, CICs (circulating immune complexes), phagocytic capacity of neutrophils (latex-stimulated) and hormones (ACTH, cortisol, TSH, thyroxine, triiodothyronine).

Results: All infants showed depression of cellular immune, humoral immune response, CIC increase and enhanced phagocytic capacity of neutrophils. Depression of cellular immune declared itself in decreased level of CD3 + (47.8%) and CD4 + (28.3%) cells, total amount of CD8 + lymphocytes increased (26.9%), while (CD4/CD8) immunoregulatory index decreased at 1.05.

Lymphemia was accompanied by development of double-positive CD4 + CD8 + immature lymphocytes (7.4%). The highest level of T-cell lymphemia was revealed among infants with Thyromegaly - 3.16, with no Thymomegaly - 2.69, intact - $1.8*10^9$/l.

At fastigium the infants with acute obstructive bronchitis and no Thymomegaly showed significant elevation of ACTH (44.6) and moderate elevation of cortisol (368.8). Intact infants: 15.8 pmol/l

and 326.1 pmol/l. Most infants with Thymomegaly showed lowest level of ACTH (41.3) and significant depletion of cortisol level (259.5). Infants with Thymomegaly showed the most significant TSH elevation (4.2) and depletion of triiodothyronine (1.17). No Thymomegaly 3.7 ME/l and 1.49 nM/l, intact 1.74 and 1.92. Thyroxine level was equal among both infected and intact infants.

Conclusion: Acute obstructive bronchitis among infants with Thymomegaly is accompanied by T-cell lymphemia and development of double-positive CD4 + CD8 + immature lymphocytes with underlying depletion of cortisol, thyroxin and elevation of ACTH. ACTH level is higher than that of intact infants, but is lower compared to infants with acute obstructive bronchitis and no Thymomegaly.

TP1066 | Elevated levels of periostin, IL-13, and TGF-β1 in the bronchoalveolar lavage fluid of patients with idiopathic eosinophilic pneumonia

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Background: Periostin is an extracellular matrix protein belonging to the fasciclin family. Periostin is also reported as a matricellular protein involved in chronic allergic diseases such as asthma and atopic dermatitis, and plays an important role in tissue remodeling and fibrosis of the lung. Periostin is induced in bronchial epithelial cells and fibroblasts by various stimuli such as interleukin (IL)-13 and transforming growth factor (TGF)-β_1, binds to cellular receptors such as integrins, and activates cells. The role of periostin in the pathogenesis of eosinophilic lung diseases, however, is unclear. To examine the contribution of periostin to eosinophilic inflammation of the lung in humans, we evaluated periostin, IL-13, and TGF-β_1 levels in the bronchoalveolar lavage fluid (BALF) of patients with eosinophilic pneumonia (EP).

Method: Periostin, IL-13, and TGF-$\beta_1$concentrations in the BALF were measured by enzyme-linked immunosorbent assay in patients with acute EP, chronic EP, idiopathic pulmonary fibrosis (IPF), and sarcoidosis. Further, we analyzed the relationship between periostin, IL-13, and TGF-β_1, levels and the number of inflammatory cells in the BALF.

Results: The absolute number of eosinophils, and the periostin, IL-13, and TGF-β_1 levels in the BALF were significantly higher in patients with EP than in patients with IPF and sarcoidosis. Concentrations of periostin significantly correlated with the concentrations of TGF-β_1, but not those of IL-13, in the BALF of patients with EP. Periostin levels also significantly correlated with the absolute number of eosinophils in the BALF of patients with IPF, but not EP. Furthermore, periostin levels in the BALF significantly correlated with the absolute numbers of CD4 + T cells in patients with EP, but not IPF. TGF-β_1 levels significantly correlated with the absolute numbers of eosinophils in the BALF of patients with AEP, but not in those with CEP and IPF. TGF-β_1 levels in the BALF also significantly correlated with the absolute numbers of CD4 + T cells in patients with EP, but not in patients with IPF.

Conclusion: The findings of the present study suggest that TGF-β_1 mainly contribute to the production of periostin in the lungs of patients with EP. Periostin might contribute to the accumulation of eosinophils into the lung in patients with IPF, but not EP.

TP1067 | Pharmacological analysis of T cell-induced bronchoconstriction in vitro and in vivo

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Background: To investigate a role of helper T (Th) cells in asthma, T cell-transfer model was analyzed for late phase asthmatic responses (*in vivo*). Culture supernatants of activated T cells were analyzed for the constriction of cultured bronchial smooth muscle cells (*in vitro*).

Method: Ovalbumin (OVA) specific Th clones were derived from either the regional lymph nodes of Balb/c mice immunized with OVA/CFA or splenocytes of DO11.10 transgenic mice expressing T cell receptor specific for OVA/H-2d. Th clones were adoptively transferred into unprimed mice. Upon antigen challenge, airway resistance was continuously monitored by either unrestrained whole body plethysmography (BUXCO) or resistance/compliance analyzer under anesthetized condition. Bronchoalveolar lavage was performed 48 hr after antigen challenge. Supernatants of stimulated Th clones were analyzed for contractile activity using collagen gels embedded with murine primary bronchial smooth muscle cells. Effects of glucocorticoid and antagonists were analyzed both *in vitro* and *in vivo*.

Results: When unprimed mice were transferred with Th clones, T5-1, T6-2, T6-4, and T6-7, Penh values were significantly increased 6 hr after OVA challenge. In contrast, mice transferred with other Th clones, BF7, T6-1, or T6-10 did not show any change. Airflow limitation was confirmed by a direct measurement of airway resistance under anesthetized, restrained, and intubated conditions. Contractile activity was detected in the supernatants of T6-2 stimulated with immobilized anti-CD3. T cell-induced contraction was not affected by dexamethasone, H1R or LTR1 antagonist.

Conclusion: T cell activation caused airflow limitation in addition to eosinophilic inflammation, AHR, and mucous hyperplasia. T cell-derived bronchoconstriction seems a good target for treatment-resistant asthma.

TP1068 | Development of experimental allergic asthma using ragweed pollen extract

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Background: The aim of this study was to develop a mouse model of allergic asthma using allergen ragweed pollen extract (W1).

Method: BALB/c mice were divided into 6 groups. Group 1 was i.p. immunized with mixture of W1 (100 μg) and $Al(OH)_3$ (2 mg) per mouse 3 times in two week intervals and challenged on days 49, 50, 51, 52, 53 by aerosol administration with W1 only. Groups 2 and 3 were i.p. immunized with W1 only (100 μg and 150 μg, respectively) 3 times in two week intervals and challenged by the same manner. Groups 4 and 5 were s.c. immunized with 100 μg and 150 μg W1, respectively. Group 6 was used as a negative control where mice were immunized and challenged with PBS only. 24 hours after the final challenge airway hyperresponsiveness (AHR) to methacholine was measured by whole body plethysmography. 48 hours after the final challenge bronchoalveolar lavage (BAL) was collected for cells differential count and lungs were removed for histological examination. W1-specific serum IgE-, IgG1- and IgG2a- antibodies were detected by ELISA.

Results: The anti-W1 IgE was at high level in all experimental groups in comparison to control group 6. At the same time in groups 1, 3, 5 anti-W1 IgE was lower than that of groups 2 and 4. W1-specific IgG1 production in groups 1, 2, 3, 4, 5 was higher than that of group 6. The anti-W1 IgG2a was at highest levels in group 2. AHR in groups 1 and 4 was higher than that of PBS mice but did not differ from each other. Analysis of cell composition in BAL demonstrated an increase of eosinophils in group 5 compared with other groups. General presentation of allergic inflammation in the lungs of mice groups 1-5 was more pronounced as compared with control group. Peribronchial and perivascular infiltration with eosinophils in groups 1, 2, 4, 5 was significantly increased in compare with control group 6.

Conclusion: The data presented in this report indicate that the group 5 protocol of allergic asthma induction is the most acceptable. The developed mouse model of allergic asthma can be a relevant model for testing of new approaches for treatment or prevention of allergic bronchial asthma.

MONDAY, 3 JUNE 2019
TPS 26
ATOPIC DERMATITIS: CLINICAL ASPECTS

TP1070 | Effect of oral steroid treatment on alarmin expression of mast cells in the dermis of patients with moderate-to-severe atopic dermatitis

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Background: Epithelial cell-derived cytokines are critical regulators in the pathogenesis of atopic dermatitis; however, mast cells are also reported to be a rich source of TSLP and IL-33 in allergic disease. We examined the effect of treatment with prednisolone on mast cell expression of TSLP and IL-33 in skin biopsies obtained after intradermal allergen challenge from patients with atopic dermatitis.

Method: Sixteen patients with moderate-to-severe atopic dermatitis washed out of systemic medications for 30 days, and randomized (1:1) to placebo or prednisolone for 5 days at 0.75 mg/kg, 5 days at 0.5 mg/kg and 5 days at 0.25 mg/kg. Intradermal challenges with allergen and saline control were conducted before and after treatment, and skin biopsies were collected from the site of challenge 24 hours post-challenge. Biopsies were stained with DAPI and immunofluorescent antibodies to tryptase/TSLP or tryptase/IL-33. Images were obtained and analysed by selecting regions of interest, and mast cells co-localizing each alarmin were counted manually and expressed as number of cells per mm^2 of the area examined.

Results: At baseline a low proportion of mast cells in the dermis expressed TSLP or IL-33. In saline-challenged biopsies, prednisolone reduced the number of mast cells expressing TSLP and IL-33 by over 3-fold compared to no reduction by placebo ($P > 0.05$). Intradermal allergen challenge increased the number of mast cells expressing TSLP and IL-33 by 10-fold and 7-fold, respectively. In allergen-challenged biopsies after prednisolone treatment there was a 37-fold decrease in the number of mast cells expressing TSLP (versus no change after placebo, $P = 0.07$) and a 3-fold decrease in IL-33 which was not different than placebo ($P = 0.96$).

Conclusion: In this small study, we observed a trend for prednisolone treatment to reduce the number of mast cells expressing TSLP after an intradermal allergen challenge. IL-33 expressing mast cells, however, was reduced but with no difference between prednisolone and placebo treatment. These data suggest that mast cell expression of TSLP after exposure to allergen may be regulated by steroid treatment.

TP1071 | The effect of steroid treatment on eosinophil progenitors, eosinophils and basophils in the skin of patients with moderate-to-severe atopic dermatitis

Price E; Al-Sajee D; Krisna SS; Munoz C; Howie K; O'Byrne PM; Lima H; Sehmi R; Gauvreau GM

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Background: Local eosinophilia is thought to contribute to disease progression in patients with atopic dermatitis, and steroid treatment is effective in part by reducing eosinophil levels in skin. We have previously demonstrated an increase in eosinophil lineage-committed progenitors (EoP) in skin during the late cutaneous response after intradermal allergen challenge; however, it is not known whether EoP are responsive to steroid treatment. This study examined the effect of prednisolone treatment on EoP levels in skin after intradermal challenge.

Method: Sixteen patients with moderate-to-severe atopic dermatitis were washed out of prescription medications for 8 days, then randomized to receive prednisolone or placebo (1:1) for 5 days at 0.75 mg/kg, 5 days at 0.5 mg/kg and 5 days at 0.25 mg/kg. Before treatment and after 7 days of treatment, patients underwent intradermal challenges with allergen and saline control, and punch biopsies were obtained from the site of challenge 24 hours later. H&E staining was performed for eosinophil counts and immunofluorescence staining was performed for EoP (CD34 + ve/IL-5Ra+ve/Von Willebrand factor-ve) and basophils (2D7 + ve). Cells were measured in the papillary dermis using Nikon Imaging Software Analysis, and compared between prednisolone and placebo groups.

Results: All patients developed a late phase cutaneous response to intradermal allergen challenge with the level of basophils, eosinophils and EoP significantly increased compared to saline control (all $P < 0.02$). Prednisolone treatment inhibited the allergen-induced increase in eosinophils by 90% and basophils by 53%, and this was statistically significant compared to placebo ($P = 0.008$ and $P = 0.013$, respectively). In contrast, EoP levels were 2-fold higher in allergen-challenged skin compared to pre-treatment levels, and significantly higher than placebo ($P = 0.028$). With saline challenge there was no change in EoP levels before and after prednisone, and no difference between prednisone and placebo.

Conclusion: These results confirm steroid sensitivity of mature eosinophils and basophils and extend these findings to show that steroid treatment does not reduce the level of eosinophil lineage-committed progenitors in allergen-challenged skin of patients with atopic dermatitis. In fact, EoP levels were even higher after

intradermal allergen challenge in skin of the patients on prednisolone treatment, but whether or not these cells are actively contributing to the T2 cytokine microenvironment is not known.

TP1072 | Activated leukocyte cell adhesion molecule modulates Th2 immune response in atopic dermatitis

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Background: Activated leukocyte cell adhesion molecule (ALCAM), a member of the immunoglobulin superfamily, is highly expressed on dendritic cells (DCs). ALCAM and its receptor CD6 are co-stimulatory molecules in the immunologic synapse; their interaction is required for T cell activation. While atopic dermatitis (AD) is recognized as a type 2 helper T cell (Th2)-mediated allergic disease, the role of ALCAM in its pathogenesis is unclear.

Method: We addressed this using an ovalbumin-induced AD mouse model. Chemokines and barrier genes were evaluated using real time-qPCR. Total IgE was measured by enzyme-linked immunosorbent assay (ELISA). Skin ALCAM expression was assessed by immunohistochemistry and flow cytometry.

Results: Serum ALCAM levels were elevated in wild-type (WT) AD mice as well as in pediatric AD patients. And ALCAM expression was increased in skin DCs of the AD mice than in the control mice. In $ALCAM^{-/-}$ mice, Th2 type cytokine production, AD symptoms, and $CD4^{+}$ effector T cell accumulations were decreased compared to WT mice. Moreover, ALCAM was linked to lower expression of skin barrier genes and number of lamellar bodies.

Conclusion: These findings indicate that ALCAM contributes to AD pathogenesis by meditating a Th2-dominant immune response and disrupting the barrier function of the skin.

TP1073 | Impact of VOC emissions from pine wood on inflammatory skin disease

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Background: In recent years, the prevalence of atopic dermatitis (AD) has risen considerably and increased indoor exposure to volatile organic compounds (VOCs) has to be considered as a potential sensitization factor. The aim of our study is to investigate the potential influence of short-term exposure to different concentrations of VOC emissions from pine wood (*Pinus sylvestris L.*), as a particularly high emitter of VOCs, on the development of skin allergic and non-allergic inflammation using two different murine models of AD.

Method: Pine wood plates were inserted in the bottom of mouse cages and VOC concentration was determined by sampling onto TENAX TA followed by thermal desorption and analysis by capillary gas chromatography/mass spectrometry. To induce an AD-like inflammatory skin disease, ears of mice were treated either with Calcipotriol or with Oxazolon. Control animals were treated with ethanol. Body weight, ear swelling and transepidermal water loss (TEWL) were monitored over the whole treatment period. A histopathological and an immunological analysis of mouse ears was performed at the end of the experiment.

Results: Application of Calcipotriol or Oxazolon induced AD-like histopathological changes leading to an increase in ear swelling and in TEWL compared to control animals. Diseased skin showed a dominant Th2 immune response, granulocyte infiltration and upregulated alarmins, such as TSLP and IL-33. Exposure to high VOC emissions (> 10 mg/m³) led to a marked increase of ear swelling and TEWL, but had no impact on the immunological response. Exposure to lower VOC emissions (5 mg/m³) had no effects in Calcipotriol-treated animals, but showed a significant reduction of TEWL, ear swelling and inflammatory markers in Oxazolon-treated animals. VOC emissions had no effects on healthy controls animals.

Conclusion: Taken together, our data suggest that diseased skin is more susceptible to exposure to emissions from pine wood compared to healthy skin. VOC emissions at high concentrations may aggravate the AD-like status. Lower emissions showed a beneficial effect, resulting in reduced development of AD. Further experiments are planned to consolidate these first findings and to evaluate the molecular mechanisms which trigger these adverse and beneficial effects.

TP1074 | Infantile atopic dermatitis: Serum vitamin D, TARC and periostin levels and their relationship with disease phenotype and clinical severity

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Background: Several markers that influence the clinical course of atopic dermatitis (AD) have been investigated so far. It has been shown that Vitamin D affect Treg cells and immune responses. Periostin, an extracellular protein that is induced by Th2-related cytokines, and TARC, also a Th2-related cytokine, increases in various atopic diseases. The aim of this study was to investigate the effect of vitamin

D, periostin and TARC levels on the severity of disease in infantile atopic dermatitis phenotypes.

Method: Atopic dermatitis patients (n = 160) with age and sex matched healthy controls (n = 79) were included in the study who applied between 2016-2017 to Department of Pediatric Allergy in Hacettepe University Faculty of Medicine. The diagnosis of AD was made according to the Hanifin-Raijka criteria. The objective SCORAD index was used for the assessment of disease severity.

Results: One hundred sixty patients(male 71.9%)with AD were included in the study. The median age of onset of symptoms was 2.0 (1.0-3.5) months (male 71.9%). The symptoms were started at head 76.9%, neck 6.9%, extremities 7.5% and body 8.8%. 39.9% of the patients were found to be atopic. Food allergy was found in 39.4%. The median objective SCORAD index was found to be 27.5 (17.5-40.0) in the whole group. In AD group, periostin and TARC levels were significantly different compared to the control group ($P < 0.001$). There was a significant correlation between objective SCORAD and TARC values in subjects with AD ($r = 0.363$, $P < 0.001$). As the severity of AD increased, vitamin D levels decreased (p for trend 0.015) and TARC values increased (p for trend < 0.001). The presence or absence of atopy did not differ in terms of TARC, periostin and vitamin D levels.

Conclusion: In infants with AD, disease severity is directly related with TARC levels; and inversely proportional to Vitamin D levels. Both periostin and TARC levels differ between patients and healthy controls. The presence of atopy has not been shown to have a significant effect on these markers.

TP1075 | Microbiological findings on skin specimens in patients with atopic eczema

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Background: Skin eczema is very often in general pathology of patients with allergic diseases. Skin eczema significantly affects the quality of life of the patient. The most common allergens were substances widespread present in any environment. PRICK tests shown that all type of allergen was accused for atopic eczema, inhaled, food allergen, fungi and allergen of workplace. It is known that disruption of basal layer of epithelial cells of skin enable passing of allergen into subcutaneous space, were microphages and dendritic cells are placed, so, sensibilization could start. Whether chronic inflammation with positive microbiological finding of specimen of affected skin is with increased risk for eczema formation is the aim of this paper.

Method: Results of microbiological analyzes of the specimens obtained from eczema, directly of affected site, were shown in this paper. PRICK test was performed for standard respiratory, food contact allergens as well as the allergens of the workplace.

Results: We analyzed specimens of 67 patients with eczema. Positive results were shown in 21 patients. The most common was staphylococcus epidermidis (7 cases), staphylococcus aureus (3 cases), Escherichia coli (2 cases), Pseudomonas aeruginosa (1 cases) Acinetobacter species (2 cases) Candida albicans (6 cases), Aspergillus fumigatus (1 case). PRICK test was positive in 46 out of 67 patients, in some of them with multiple microbes. The most common positive allergens were dermatophagoides pteronyssinus (18 cases), ambrosia (7 cases) Candida albicans (14 cases), aspergillus fumigates (6 cases), Aspergillus niger (4 cases). Trees (5 cases), Grass (4 cases). Total IgE were elevated in 45 out of all 67 patients (mean 346 IU/L (±93), Measurement of specific IgE were performed for ambrosia (mean 16.6 IU/L, ±8.2), dermatophagoides 11.5 IU/mL (±5.4) aspergillus fumigates (4.2 IU/mL (±2.5), candida albicans 4.1 IU/mL (±1.9). The coincidence of PRICK tests and microbiological analyzes was most often present in fungi. The patients were treated locally with antifungal medication, and by specific immunotherapy, when appropriate.

Conclusion: We shown substantial correlation between results of analyzes of microbiological skin swab and allergologic examination performed by PRICK test. Both results were used in consideration for prescription of specific immunotherapy as well as local or systemic use of antibiotic or fungicides.

TP1076 | Epidermal lipid and skin microbiome composition are altered in Korean patients with atopic dermatitis

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Background: We investigated whether the profile of stratum corneum (SC) lipid and skin microbiome composition are altered in patients with atopic dermatitis (AD) compared to healthy subjects.

Method: Skin samples were obtained using skin tape stripping from 35 patients with AD and 26 healthy subjects matched for age and sex. Proteins and lipids of SC from nonlesional and lesional skin of AD patients and normal subjects were quantified by mass spectrometry. Skin microbiome profile was analyzed using bacterial 16S rRNA sequencing.

Results: Filaggrin degradation products (FDP: cis-urocanic acid, trans-urocanic acid, and pyroglutamic acid) were lower in nonlesional

and lesional skin of AD patients than those of normal subjects in both adults and children (all $P < 0.05$). Nonlesional and lesional SC of AD subjects showed an increased proportion of short-chain (N-14:0 to N-22:0) NS ceramides, lysophosphatidylcholines (14:0-20:0 LPC), and sphingomyelins with a simultaneous reduction in the proportion of corresponding long-chain species when compared to normal subjects. The absolute amounts of EOS ceramides and the ratios of EOS ceramide to 16:0 NS ceramide were also decreased in lesional SC from AD patients compared to nonlesional SC from AD subjects and normal subjects in both adults and children. Ratio of long-chain to short-chain LPC was negatively correlated to SCORAD and transepidermal water loss (TEWL) in AD patients. Ratios of long-chain to short-chain NS ceramides and EOS ceramide to 16:0 NS ceramide also showed negative correlation with TEWL. In children, lesional and nonlesional skin of AD patients displayed an increased abundance in *Staphylococcus* compared to nonlesional skin of AD patients and normal subjects, respectively. In addition, *Actinomycetales*, *Streptococcus*, *Bacteroides*, *Lachnospiraceae*, *Pasteurellaceae*, *Faecalibacterium*, *Bacillales*, *Bifidobacterium*, and *Dolosigranulum* were positively correlated to levels of FDPs and long-chain NS ceramides, while *Staphylococcus* was negatively correlated to levels of FDPs and long-chain NS ceramides in adult healthy subjects.

Conclusion: Our results suggest that both lesional and nonlesional skin of AD patients show an altered epidermal lipid composition and microbial configuration in Korean adult and pediatric patients with AD.

TP1077 | Maternal and paternal atopy and risk of eczema in early infancy: A sex-stratified analysis of a large cohort

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Background: Parental atopic disease is a major risk factor for atopic dermatitis (AD), but it is unclear if the effect is dependent on the sex of the child. In this study, we aimed to investigate if maternal or paternal atopy in general and AD specifically had differential associations with infant eczema in their daughters or sons.

Method: From the PreventADALL (Preventing Atopic Dermatitis and Allergies) randomized control trial in a mother-child birth cohort study recruited during pregnancy in Norway and Sweden, we included 1146 control infants, born at gestational week 35 or later, who were not randomized to the early skin care intervention. Information on maternal and paternal atopic disease was obtained by questionnaires addressed to the mothers at 18 and 34 weeks of pregnancy. Maternal and paternal atopy was defined as reporting having or having had a doctor diagnosis of AD, allergic rhinoconjunctivitis, asthma, or food allergy. Study visits were conducted at age three and six months. Eczema was defined as the presence of eczematous lesions observed by study personnel, excluding differential diagnosis to AD. The possibility of confounding variables influencing parental AD and offspring eczema were considered to be low, thus unadjusted risk estimates were calculated from 2 × 2 contingency tables.

Results: At age three months, eczema was observed in 144 infants. The odds ratio (OR) of eczema was 1.58 (CI 95% 1.04-2.40) by maternal atopy and 1.49 (1.02-2.17) by paternal atopy. The corresponding ORs increased by maternal AD to ORs of 1.68 (1.00-2.83) and paternal AD to 2.03 (1.18-3.51). The effects were statistically significant in boys only, with ORs of 2.06 (1.03-4.10) and 2.11 (1.03-4.35), respectively.

At age six months, eczema was observed in 236 infants. Paternal atopy and paternal AD significantly increased the risk of eczema, with ORs of 1.39 (1.02-1.89) and 1.98 (1.25-3.14) respectively, while maternal atopy in general and AD specifically, were not associated with eczema at six months of age. The effect of paternal AD on eczema in 6-month old infants were only found in boys, with an OR of 2.48 (1.34-4.59).

Conclusion: We found that the risk of early infant eczema by parental atopy differs in boys and girls.

TP1078 | Sensitization to cockroach tropomyosin among patients with atopic dermatitis

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Background: Atopic dermatitis (AD) is a chronic, pruritic skin disorder. Prevalence of atopic dermatitis is approximately 15-30% among children and 2-10% among adults. Tropomyosin is a pan-allergen among invertebrates including mites, cockroach, shrimp and other crustacean and mollusks, and parasites, and it is implicated in IgE cross-reactivity. In Brazil, sensitization to cockroach tropomyosin (Periplaneta americana allergen Per a 7) is present in approximately 50% of patients with asthma and/or rhinitis. Therefore, in our area Per a 7 is a major allergen. Our aim was to evaluate sensitization to cockroach among patients with atopic dermatitis and its clinical implications.

Method: One hundred and twelve patients with AD, attending the Allergy or Dermatology Clinics at our Institution, were enrolled. Severity of the disease was evaluated with SCORAD. Total IgE was measured by ImmunoCAP® and specific IgE to cockroach tropomyosin (Per a 7) was quantitated by chimeric ELISA. Clinical and

immunological parameters of patients sensitized to Per a 7 were compared to those not sensitized.

Results: Patients were aged 3-67 years-old (mean ± SD 24.9 ± 1.4 years), 67% female. Specific IgE to cockroach tropomyosin was detectable in 30/112 (26.8%) patients, with levels ranging from 2.3 to 3.191 UI/mL. Total IgE levels ranged from 24.3-63 000 UI/mL (geometric mean 12 133 UI/mL). Ratios of IgE to Per a 7 to total IgE ranged from 0.03% to 33.8% (mean 5.7%). Mean SCORAD was 45.4 (± 3.3) and 40.4 (±2.1); geometric mean of total IgE levels was 3654 UI/mL and 1819 UI/mL; mean age at onset of symptoms was 11 (±2.7) and 8.9 (±1.4); mean duration of disease was 12.7 (±1.7) and 16.4 (±1.4) years, among patients sensitized or not sensitized to Per a 7, respectively. These differences were not significant. Asthma was present in 12 and 30 of patients; and rhinitis was present in 24 and 61 of patients, sensitized and not sensitized to Per a 7, respectively, with no significant differences

Conclusion: .Frequency of IgE sensitization to Per a 7 among Brazilian patients with AD was lower than that observed among patients with asthma and/or rhinitis. Although presence of IgE to Per a 7 may not be a useful biomarker for severity of AD or association with asthma and rhinitis, sensitization to this allergen may be important if considering allergen-specific immunotherapy for patients with AD.

TP1079 | Alterations in skin physiology are associated with disease severity in chilean patients with atopic dermatitis

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Background: Atopic dermatitis (AD) is a multifactorial inflammatory skin disease characterized by pruritic eczematous lesions. Skin physiological parameters are abnormal in AD patients, including transepidermal water loss (TEWL), pH and sebum content (S). Nevertheless, it is not clear how these parameters correlate with disease severity in Latin American patients. The purpose of this study is to determine the skin TEWL, pH, and S in AD Chilean patients of all ages and healthy non-atopic controls (HC), and to evaluate their correlation with disease severity evaluate by SCORAD, EASI and blood eosinophil counts in AD patients.

Method: We conducted a cross-sectional study in 58 patients with AD and 41 HC of all ages. Age groups were separated into children (C; <18 years) and adult (A). TEWL, pH, and S were quantified using Courage-Khazaka® TM300, PH905, and SM815 probes. In AD subjects, we evaluated the most severe AD lesion as "lesional area" (L) and a healthy area as "non-lesional" (NL). Forehead, cheek, antecubital fossa and forearm were assessed in HC.

Results: Mean age was 5.6 ± 5.5 years in C-AD (n = 41) and 7.7 ± 4.9 years in C-HC group (n = 6; $P = 0.39$). Mean age was 27 ± 9 in A-AD (n = 17) and 29 ± 6 (n = 27; $P = 0.4$) in A-HC. Median TEWL was significantly different between L, NL, and HC skin in C (L: 59.7 g/hm^2; NL: 21.8 g/hm^2; HC: 15.5 g/hm^2, $P < 0.001$) and in A (L: 64.7 g/hm^2; NL: 17.6 g/hm^2; HC: 15.1 g/hm^2, $P < 0.001$). Median pH was significantly higher in L areas, both in C (median pH L: 5.0; NL: 4.4; HC: 4.3, $P = 0.001$) and A (pH L: 4.8; NL: 4.3; HC: 4.3, $P = 0.01$). Regarding S, there were no significant changes in C (L: 1 μg/cm^2; NL: 0 μg/cm^2; HC: 1.25 μg/cm^2; $P = 0.25$), but we found a significant decrease in S of NL and L areas of A-AD subjects compared to A-HC (L: 1 μg/cm^2; NL: 0 μg/cm^2; HC: 29.3 μg/cm^2; $P < 0.001$). In AD patients, L and NL TEWL positively correlated with SCORAD and EASI scores (L vs SCORAD $r = 0.46$, $P < 0.01$; L vs EASI $r = 0.4$, $P < 0.01$; NL vs SCORAD $r = 0.3$, $P < 0.05$; NL vs EASI $r = 0.37$, $P < 0.01$). Skin pH of L areas was significantly correlated to TEWL-L ($r = 0.4$, $P < 0.01$) and SCORAD ($r = 0.35$, $P < 0.05$). S content was not associated with SCORAD or EASI severity scores. L and NL TEWL, pH, and S were not associated with blood eosinophil counts.

Conclusion: Our study is the first in Latin America to quantify the physiological skin parameters TEWL, pH, and S in children and adults with AD, confirming the epidermal alterations that characterize AD and their correlation with disease severity in Hispanic population.

TP1080 | Type 2 innate lymphoid cells (ILC2s) are reduced in lesional skin biopsies from subjects with atopic dermatitis (AD) following treatment with oral corticosteroids

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Background: Atopic dermatitis (AD) is characterised by chronic relapsing inflammation of the skin, with pruritic and eczematous lesions. Pro-inflammatory cells including CD4 + T-cells, and type 2 innate lymphoid cells (ILC2s) are proposed to be critical drivers of type 2 inflammation characteristic of AD. This study investigated the effect of oral corticosteroids treatment on these cells in lesional skin.

Method: Sixteen subjects (18-65 yrs) diagnosed with moderate-to-severe AD were enrolled in a double-blind, placebo-controlled study. After an 8-day washout period, subjects were randomized 1:1 to receive prednisolone (5 days at 0.75 mg/kg, 5 days at 0.5 mg/kg and 5 days at 0.25 mg/kg) or placebo. Pro-inflammatory cells in lesional skin biopsies extracted by enzymatic digestion and blood were enumerated by flow cytometry pre- and 7 days post-treatment. Live, singlet CD45 + cells were identified as ILC2s

(Lin-CD127 + CD294 +), CD4 + T-cells (Lin+CD4 +) and basophils (Lin+HLA-DR-CD123 +). Physician reported outcomes (EASI, SCORAD and IGA) and patient reported outcomes (POEM and DLQI) and were assessed before and after 7 days of treatment. Statistical analyses of data were performed using non-parametric tests.

Results: There was a significant reduction in total ILC2s and basophils extracted from lesional biopsies following steroid (2.5 fold and 8 fold, respectively, $P < 0.05$) but not placebo treatment. In contrast, steroid treatment had no effect on ILC2 numbers in blood. Steroid but not placebo treatment significantly reduced total CD4 + T cells numbers in blood (1 fold, $P < 0.05$) but not lesional skin. There was a significant improvement in all physician and patient reported symptom scores following steroid compared to placebo treatment ($P < 0.05$).

Conclusion: Our data indicate that prednisolone treatment in subjects with atopic dermatitis is associated with a reduction in ILC2s and basophils in lesional skin and improvement in patient clinical scores. Targeting ILC2 activation may be important to control chronic inflammation in the skin in atopic dermatitis. Long-term use of steroids confers adverse side effects therefore blocking factors that directly activate ILC2s in the skin may provide alternate therapies for this condition.

TP1081 | Serum level of IL-19 and pro-inflammatory cytokines (IL-17A, IL-4 And IL-1β) in children with atopic dermatitis - the role and association with disease severity

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Background: Interleukin-19 (IL-19) is known as a pro-inflammatory cytokine produced mainly by monocytes and keratinocytes and stimulated by IL-4, IL-13 and IL-17. IL-19 promotes the development and function of Th2 cells and thus can play a role in pathogenesis of allergic diseases. However, no clinical studies have analyzed serum levels of IL-19 in larger series of children with atopic dermatitis (AD). This study was performed to clarify whether serum levels of IL-19 and cytokines associated with IL-19 are reflecting on disease severity.

Method: Children diagnosed with atopic dermatitis in the active phase of the disease and healthy children were enrolled in the study. The diagnosis of atopic dermatitis was made by a physician according to criteria by Hanifin and Rajka. Demographic data including age, gender, sex, family history of atopy, age of onset, plasma eosinophil level were recorded. Disease severity was measured by SCORAD index. IL-19 plasma levels were measured with human IL-19 ELISA kit (R&D Systems), IL-17A, IL-4 and IL-1β plasma levels were measured with flow cytometry (CBA Human Enhanced Sensitivity Mater Buffer Kit, BD Biosciences), according to manufacturers' instructions.

Results: The study consisted of 23 children with atopic dermatitis and 12 healthy children (with mean age 5.91 years ± 3.61 and 8.56 ± 4.89, respectively, $P < 0.05$). Mean IL-19 plasma level was 61.1 pg/mL ± 105.7 in AD patients and 2.1 ± 5.9 pg/mL in healthy controls. Mean levels of all cytokines in AD children were also elevated in comparison to healthy controls (129.4 fg/mL ± 86.1 vs 18.8 fg/mL ± 36.6 for IL-17A; and 67 fg/mL ± 82.8 vs 8.9 fg/mL ± 31 for IL-1β, respectively) ($P < 0.05$); however, cytokine levels were not significantly correlated with SCORAD index. IL-4 plasma levels did not differ significantly between AD and control group. Overall IL-19 levels were significantly increased in patients in the top quartile of SCORAD (mean 47.8) compared to those in the bottom quartile and the control group (ANOVA, $P < 0.001$ for all four comparisons).

Conclusion: Plasma IL-19 level was found to be significantly elevated in children with high SCORAD. Our findings indicate that serum IL-19 may play a role in AD pathogenesis and become a novel indicator for evaluating disease activity.

TP1082 | Comparative analysis of fragrance haptens in emollients available in Poland and Spain

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Background: Atopic dermatitis is the most common chronic inflammatory skin disease among pediatric patients. It affects up to 20% of children worldwide. Characterized by pruritus and eczema, it is also associated with improper skin barrier function and allergen sensitization. As emollients and moisturizers are considered AD's basic therapy, the aim of our study was to assess the presence of fragrance haptens in such products available in Poland and Spain.

Method: We created a database of emollients developed for atopic skin care available in most popular online pharmacies, both in Poland and Spain. To evaluate the frequency of allergenic fragrances we compared their composition with 139 contact allergens listed in the European Baseline Series (EBS), the Fragrance Series and the Cosmetic Series.

Results: As of December 2018, our list comprised 160 and 111 emollients available on Polish and Spanish market respectively. Ingredients could not be determined in 28 (17.5%) products in Poland and in 24 (21.6%) in Spain. Only 24 (18.2%) and 12 (14.9%) products were hapten free, while the remaining 108 (81.8%) and

74 (85.1%) emollients contained at least one contact allergen. In 31 (23.48%) products in Poland and in 32 (36.78%) in Spain there was at least one fragrance component, the maximum number being 8 and 10 fragrance haptens per product respectively. In both groups of emollients, the most common fragrance ingredient and the fourth most common ingredient overall, was undefined perfume, present in 28 (25.9%) emollients in Poland and in 31 (41.3%) in Spain. It was followed by Benzyl Alcohol 9 (8.3%), Linalool 3 (2.8%) and Benzyl Salicylate 2 (1.9%) in Poland, whereas in Spain, Linalool 6 (8.0%), Benzyl Alcohol 5 (6.7%) and Geraniol 4 (5.3%).

Conclusion: The study shows that great majority of products taken into consideration, contain at least one potential contact allergen listen in the EBS, the Cosmetics and Fragrance Series. What draw our attention was a high number of fragrance components that have no other function than to improve customer's response. As the function of skin barrier is impaired, which allows allergen's permeation, the possibility of sensitization to fragrance substances cannot be excluded. These findings indicate a need for patient education about potentially allergenic ingredients, stronger cooperation between academia and cosmetic manufacturers and further research into mechanism of contact dermatitis in patients with atopic dermatitis.

TP1083 | The use of probiotics in topical treatment of atopic dermatitis – a systematic review

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Background: Atopic dermatitis (AD) due to its chronic course requires regular application of emollients on the skin, which rebuilds its impaired barrier function. Recently, there has been an increasing interest in promising, effective topical therapies. These therapies derive from the fact that the underlying pathology of AD involves not only the impaired skin barrier function but also the immune dysregulation, susceptibility to *Staphylococcus aureus* skin infection, and cutaneous dysbiosis. The purpose of this study was to review the extent and effectiveness of interventions with topical usage of probiotics in AD patients.

Method: We have searched for randomized controlled trials (RCTs) that compare the topical application of probiotics with any standard procedures or no intervention as a control, in PubMed, Embase, the Cochrane Reviews, and Cochrane Trials databases (January 1980 – December 2018). Trials published solely in abstract form were excluded because the methods and results could not have been fully analyzed. All trials included in the review had to be performed on patients with atopic dermatitis.

Results: Six relevant RCTs were identified. Although the trials were performed on heterogenous populations and different types of probiotics using unique application techniques, all the gathered data proved efficacity of the experimental treatment in measurable ways, e.g. Scoring Atopic Dermatitis Index (SCORAD) and modified Eczema Area and Severity Index (mEASI). Moreover, there were no significant adverse effects reported in any of the studies reviewed. The bacteria used in those interventions included *Lactobacillus johnsonii*, *Roseomonas mucosa*, *Staphylococcus epidermidis*, *Staphylococcos hominis*, *Lactobacillus sakei, and Vitreoscillia filiformis*.

Conclusion: There is a growing interest in the potential application of probiotics in managing various inflammatory diseases, including allergies. There are attempts underway to implement this innovative approach into clinical practice. The RCTs report that even topical application of proper bacteria can alter the skin microbiome, contributing to the stabilization of a disturbed balance of the microbiome observed in the AD patients.

TP1084 | Dupilumab is very effective in a large cohort of difficult-to-treat adult atopic dermatitis patients: First clinical and biomarker results from the Bioday registry

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Background: Dupilumab has shown promising results in phase III trials and has recently been approved for the treatment of moderate to severe atopic dermatitis (AD) in adults. At this moment, daily practice data on dupilumab treatment are lacking. The objective of this study was to study the effect of dupilumab treatment on clinical efficacy and serum biomarkers in adult patients with moderate to severe AD in daily practice.

Method: Data were extracted from the Bioday registry. Sixteen and 28-weeks clinical effectiveness of dupilumab was expressed as number of patients achieving EASI-50, EASI-75 as well as patient reported outcome measures (POEM, DLQI, NRS-itch). Twenty-nine biomarkers representing different disease pathways were measured in 35 patients treated with dupilumab without concomitant use of oral immunosuppressive drugs at 5 different time points (baseline, 4 weeks, 8 weeks, 12 weeks and 16 weeks).

Results: In total, 153 patients treated with dupilumab in daily practice were included. The mean percent change in EASI score was 74% after 16 weeks and 76% after 28 weeks of dupilumab treatment. The EASI-50 and EASI-75 were achieved by 125 (86%) and 93 (64%) patients at week 16 and 130 (90%) and 100 (69%) patients after 28 weeks of treatment. The proportion of patients achieving a clinically meaningful response expressed as the proportion of patients achieving EASI-75 or NRS ≥ 4-point improvement or DLQI ≥ 4-point improvement after 16 weeks of dupilumab treatment was 89%. The

most reported side effect were conjunctivitis in 55 (36%) and eosinophilia in 73 (51%) patients. Dupilumab significantly decreased type 2 and severity serum biomarkers including, CCL17(TARC), CCL18(PARC), periostin and IL-22.

Conclusion: Sixteen and 28 weeks of dupilumab treatment was very effective in a large majority of patients with very difficult-to-treat AD in a daily practice setting. The most reported side effect in this daily practice cohort was conjunctivitis. Dupilumab significantly suppressed Th2 and severity related serum biomarkers.

TP1085 | Dupilumab in adolescents with moderate-to-severe atopic dermatitis and a history of allergic rhinitis: Subgroup analysis from a randomized phase 3 trial

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Background: Dupilumab is a fully human anti-interleukin (IL)-4Rα monoclonal antibody that inhibits signaling of IL-4 and IL-13, Th2 cytokines involved in atopic/allergic diseases such as atopic dermatitis (AD) and allergic rhinitis (AR). Dupilumab is approved for treatment of adults with inadequately controlled moderate-to-severe AD in several countries. Recently, dupilumab demonstrated efficacy in a phase 3 trial in adolescents with moderate-to-severe AD (AD-1526: NCT03054428). The objective of this subgroup analysis was to determine if a history of AR impacts the efficacy of dupilumab treatment in adolescent patients (pts) from the AD-1526 trial.

Method: In this double-blinded, placebo (PBO)-controlled, phase 3 trial, pts (12-17 years) with moderate-to-severe AD inadequately controlled with topical therapies were randomized 1:1:1 to dupilumab 300 mg every 4 weeks (q4w): dupilumab 200 mg or 300 mg every 2 weeks (q2w): PBO q2w, for 16 weeks (Wks). Efficacy endpoints included proportions of pts with Investigator's Global Assessment (IGA) 0 or 1, ≥75% improvement from baseline (BL) in Eczema Area and Severity Index (EASI-75), and ≥ 4-point improvement in peak pruritus numerical rating scale (NRS).

Results: A large proportion of pts reported history of AR at BL (60%/72%/67% in the q4w/q2w/PBO groups, respectively). At Wk16, more pts receiving dupilumab treatment vs PBO (q4w/q2w vs PBO; q4w/q2w difference vs PBO [95% confidence interval]) achieved IGA score 0/1 regardless of history of AR (with history of AR: 22.0%/25.4% vs 3.5%; 18.5% [6.1-30.9]/21.9% [9.8-34.0]; no history of AR: 11.8%/21.7% vs 0.0%; 11.8% [0.9-22.6]/21.7% [4.9-38.6], for the q4w/q2w groups vs PBO, respectively). Similar results were observed for proportion of pts achieving EASI-75 (with history of AR: 36.0%/44.1% vs 8.8%; 27.2% [12.0-42.4]/35.3% [20.7-49.9]; no history of AR: 41.2%/34.8% vs 7.1%; 34.0% [14.9-53.1]/27.6% [6.0-49.3], respectively). Additionally, more pts treated with dupilumab vs PBO achieved ≥ 4-point improvement from BL in peak pruritus NRS at Wk16, both in the group with (26.5%/37.3% vs 5.4%; 21.2% [7.5-34.9]/31.9% [18.3-45.6]) and without (26.5%/34.8% vs 3.6%; 22.9% [6.6-39.2]/31.2% [10.6-51.9]) a history of AR.

Conclusion: Similar to previous findings in the adult population, dupilumab improved signs and symptoms in adolescent pts with moderate-to-severe AD regardless of history of AR, implying that a potentially increased type 2 burden does not impact dupilumab efficacy.

TP1086 | Efficacy of dupilumab in adolescents with moderate-to-severe atopic dermatitis with and without comorbid asthma: Subgroup analysis from a 16-week randomized phase 3 trial

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Background: Dupilumab (DPL), a fully human monoclonal antibody that inhibits signaling of Th2 cytokines interleukin (IL)-4 and IL-13, is approved in several countries for the treatment of moderate-to-severe atopic dermatitis (AD) in adults and in the USA for moderate-to-severe eosinophilic or corticosteroid-dependent asthma in patients (pts) aged ≥ 12 years. Efficacy and safety of DPL have also been evaluated in adolescent pts (AD-1526 study: NCT03054428). The objective of this subgroup analysis was to determine whether a history of asthma impacts the efficacy of DPL treatment in adolescent pts in the AD-1526 trial.

Method: This was a randomized, double-blinded, placebo-controlled, phase 3 trial. Pts (12-17 years) with moderate-to-severe AD inadequately controlled with topical therapies were randomized 1:1:1 to DPL 300 mg every 4 weeks (q4w), DPL 200 mg or 300 mg every 2 weeks (q2w), or placebo (PBO) q2w for 16 weeks. Efficacy endpoints included proportion of pts with Investigator's Global Assessment (IGA) 0/1 (clear/almost clear), ≥75% improvement from baseline (BL) in Eczema Area and Severity Index (EASI-75), and ≥ 4-point improvement from BL in peak pruritus Numerical Rating Scale (NRS) scores.

Results: 57%, 62%, and 64% pts reported history of asthma at BL in the q4w, q2w, and PBO groups, respectively. At Week 16, a larger

proportion of pts in the DPL groups vs PBO achieved IGA score 0 or 1, regardless of asthma comorbidity (respectively, q4w/q2w vs PBO; q4w difference vs PBO [95% confidence interval (CI)]/q2w difference vs PBO [95% CI]): with asthma 14.6%/23.5% vs 3.7%; 10.9% [−0.3, 22.1]/19.8% [7.1, 32.5]; without asthma 22.2%/25.8% vs 0%; 22.2% [8.6, 35.8]/25.8% [10.4, 41.2]). Also, significantly more pts in the DPL groups vs PBO achieved EASI-75 regardless of prior asthma (with asthma 37.5%/41.2% vs 9.3%; 28.2% [12.5, 44.0]/31.9% [16.4, 47.5]; without asthma 38.9%/41.9% vs 6.5%; 32.4% [14.3, 50.6]/35.5% [16.1, 54.9]). Proportion of pts achieving ≥ 4-point improvement from BL in peak pruritus NRS at Week 16 was: with asthma 29.8%/35.3% vs 5.6%; 24.2% (9.8, 38.7)/29.7% (15.3, 44.2); without prior asthma 22.2%/38.7% vs 3.3%; 18.9% (3.9, 33.9)/35.4% (17.1, 53.7).

Conclusion: DPL improves signs and symptoms of AD in patients with and without history of asthma. This suggests that, in adolescent pts, the efficacy of DPL in moderate-to-severe AD is not affected by co-existing atopic diseases, such as asthma.

TP1087 | Microbiome stability and skin physiology in atopic eczema patients and healthy controls upon application of emollients with different PH

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Background: Whereas healthy skin has a rather acidic pH of 5.5 as part of the intact skin barrier, atopic eczema (AE) patients have a slightly higher skin pH according to previous studies. In addition, AE patients typically exhibit a disturbed skin barrier and skin microbiome. However, it is not known if a higher skin pH in AE patients is a cause, or a result, of microbiome dysbiosis.

Method: We investigated the effect of the application of emollients with either skin neutral pH (5.5) or basic pH (8.5) on skin microbiome and skin physiology, also considering AE related clinical parameters in a human study. Participants (6 AE patients, 6 healthy controls (HE)) applied the emollients twice daily for 8 weeks on opposite body sites. Once a week skin swabs for 16S rRNA NGS analysis of the V1-V3 region were taken. In parallel, skin physiology was investigated (transepidermal water loss (TEWL), hydration, pH) and AE related parameters were assessed (local SCORAD, EASI).

Results: At baseline, AE patients had higher skin TEWL and lower skin hydration, whereas no difference in pH was detected between AE and HE in this study. Over time, TEWL of AE patients treated with pH 8.5 emollient increased whereas for all other group the TEWL remained stable, whereas the Corneometer values for skin hydration seem to be independent of emollient application. Skin treated with pH 8.5 emollient developed an increased pH compared to pH 5.5 treated skin over time. At baseline, beta-diversity analysis showed a difference in global microbiome between AE and HE. Over time, the microbiome remained stable in HE and a trend for a change from baseline is seen in AE patients. Richness increased over the treatment period in AE patients. Further analysis of the microbiome changes on the different taxonomic levels is ongoing.

Conclusion: To best of our knowledge, this is the first data on frequently tracked skin microbiome over a time course of 8 weeks, investigating the influence of emollients. The increase in Richness over the treatment period hints towards a higher susceptibility of the skin microbiome of AE patients to external factors. The pH of the emollient did not affect the skin microbiome.

TP1088 | Establishment of facial atopic dermatitis with scratching (FADS) mice by deleting Ikk2 in dermal fibroblasts

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Background: Atopic dermatitis (AD) is a chronic or relapsing inflammatory skin disease characterized by persistent pruritus and recurrent eczema. To clarify its molecular mechanism, it is important to establish a mouse model similar to the phenotypes of AD patients, particularly in exhibiting scratching behavior. IKK2, a component of the IkappaB kinase complex, exerts pro-inflammatory responses, whereas its deficiency in keratinocytes paradoxically causes skin inflammation. However, it remains elusive whether impairment of the NF-kappaB pathway in keratinocytes is critical or that of adjacent skin cells can also generate inflammation. In this study, we sought to generate a mouse model exhibiting skin inflammation by which dermal fibroblasts lack IKK2 expression and evaluate whether cutaneous inflammatory phenotypes are similar to those of AD patients.

Method: To generate *Ikk2*-deficient mice (*Nestin*^{cre};*Ikk2*$^{FL/FL}$) in which IKK2 is deleted in dermal fibroblasts, we crossed female *Ikk2*$^{FL/FL}$ mice to male *Nestin*^{cre};*Ikk2*$^{FL/+}$mice. We confirmed the deletion of IKK2 in dermal fibroblasts using Rosa-RFP reporter system.

Results: *Nestin*^{cre};*Ikk2*$^{FL/FL}$ mice spontaneously developed skin inflammation limited to the face, with the appearance of IKK2-deficient RFP^{+} fibroblasts in the facial skin. These mice showed

phenotypes similar to those of AD patients, including persistent scratching behaviors. Serum IgE and periostin levels, systemic biomarkers reflecting type 2 inflammation, were significantly increased in *Nestin*^{cre};*Ikk2*$^{FL/FL}$ mice. Thus, we named these mice as Facial Atopic Dermatitis with Scratching (FADS) mice. Inflamed face skin of FADS mice showed significant increases in keratinocyte proliferation, eosinophil/mast cell infiltration, and periostin deposition. Moreover, IKK2 deletion in tissue-resident cells was required for the development of skin inflammation. Of interest, skin inflammation in FADS mice was resistant to treatment with representative AD drugs, an immunosuppressive drug, and drugs targeting Jaks or STAT3.

Conclusion: FADS mouse is a novel AD model that will be useful in clarifying AD pathogenesis and in developing a novel therapeutic agent for AD symptoms.

TP1089 | Cytokines and adipokines in serum of psoriasis patients with varying body mass index

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Background: Psoriasis, an immune-mediated inflammatory skin disease with involvement of pro-inflammatory cytokines may be impacted by white adipose tissue which activates the inflammation by production of adipokines and cytokines. This study assesses the serum levels of pro-inflammatory cytokines and adipokines in patients with psoriasis of varied body mass index (BMI).

Method: 59 patients with psoriasis with varied skin lesions and severity aged from 18 to 50 years old were assessed. Inflammatory cytokines (IL-6, IL-8, IFNγ, IL-17, IL-18 and TNFa) and adipokines (adiponectin, visfatin and chemerin) in sera of psoriasis patients and healthy volunteers (36 adults) were assayed by ELISA.

Results: Serum levels of IL-6, IL-8, IFNγ, IL-17, IL-18 and TNFa in most were higher in most psoriasis patients compared with healthy controls ($P < 0.05$). The levels of adiponectin were lower more than twice in psoriasis patients. Levels of chemerin showed a great increase in all the patients ($P < 0.001$). The level of visfatin demonstrated a high variability being decreased in 15 patients among the studied 59 patients and not correlated with control data in other patients. There was a high correlation with BMI of patients. In psoriasis patients with high BMI (26-30), the levels of all pro-inflammatory cytokines were greater than in patients with normal BMI (21-25). This high correlation was also seen between the level of serum adipokines and BMI.

Conclusion: Serum levels of the main pro-inflammatory cytokines and studied adipokines (chemerin) demonstrated an increase in psoriasis patients which correlates with the severity of disease and BMI of patients. The level of serum pro-inflammatory cytokines and studied adipokines may be used as a biomarker tool for the analysis of the response of psoriasis to treatment.

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TP1090 | Probiotic peanut oral immunotherapy (PPOIT) is effective at inducing 8-week sustained unresponsiveness after 18 months of treatment

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Background: We previously evaluated combined probiotic and peanut oral immunotherapy (PPOIT) in a double-blind placebo-controlled randomised trial in 62 children aged 1-10 years with peanut allergy. We showed that PPOIT was highly effective at inducing desensitisation (89.7% PPOIT vs 7.1% placebo, $P < 0.001$) and 2-week sustained unresponsiveness (82.1% PPOIT vs 3.6% placebo, $P < 0.001$) after 18 months of treatment. Here we report an open study evaluating 8-week sustained unresponsiveness following PPOIT therapy.

Method: 20 children aged 1-12 years with peanut allergy, confirmed by a study entry double-blind placebo-controlled food challenge (DBPCFC) to cumulative 4 g peanut protein, were enrolled. All subjects received 18 months PPOIT. Desensitisation, defined as passing a 4 g peanut protein DBPCFC at end-of-treatment, and 8-week sustained unresponsiveness (SU), defined as passing a 4 g peanut protein DBPCFC 8-weeks post-treatment, were assessed. A sensitivity analysis setting all non-treatment completers as non-responders was performed.

Results: Sixteen children (median age 8.4 years, IQR 6.3, 10.8) completed study treatment. Median baseline skin prick test wheal size was 12 mm (IQR 9-15 mm), geometric mean baseline peanut sIgE was 18.6 kU/L (95% CI 7.7-45.3 kU/L). Desensitisation was achieved in 94% (15/16) of treated subjects. 8-week SU was achieved in 75% (12/16) of treated subjects. Sensitivity analysis confirmed high clinical response rates of 75% desensitisation and 60% 8-week SU.

Conclusion: This open study confirms that PPOIT is highly effective at inducing both desensitisation and 8-week SU. A larger 3-arm multicentre randomised trial comparing PPOIT with OIT and placebo is underway to confirm these findings.

TP1091 | The literature discusses the effect of probiotics on the course of allergic diseases through the modulation of the immune response

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Background: The literature discusses the effect of probiotics on the course of allergic diseases through the modulation of the immune response.

Method: 192 children aged from 3 months to 3 years with gastrointestinal and skin food allergy (FA) were included in an open, randomized comparative study, with 122 patients in the main group, and 70 in the control group. During the monthly introductory period all patients received conventional therapy and diet. Later, in the therapy for the children of the main group there was added a multistrain probiotic(MP) that contained composition of 7 strains(L. casei, L. rhamnosus, Str.thermophilus, L.acidophilus, B.breve, B.infantis, B.longum in 10*9) and prebiotic inulin fructooligosaccharide. At the meantime, the children from the control group continued to receive initial therapy and diet. Initially and later during the treatment, patients were monitored for clinical symptoms; levels of secretory immunoglobulin A (sIgA), feces eosinophilic neurotoxin (fEDN) and calprotectin, as well as microbiological indicators.

Results: After one month of the MP treatment for the children from the main group there was noted a significant decline in the SCORAD, as well as clinical improvement of FA gastrointestinal symptoms in comparison with the children of control group. The children from both groups had reduction of the sIgA. We also observed in most patients the high level of fEDN and normal calprotectin level. The MP intervention was associated with a significant enhancement of sIgA, meanwhile in the control group this enhancement was not stated. We also found a statistically significant decrease of fEDN ($P < 0.001$) in the patients of main group .The sIgA enhancement and the fEDN decrease in children from the main group were statistically correlated with clinical improvement of their gastrointestinal and skin symptoms in comparison with the patients from the control group. All patients from both groups, prior to treatment, had the prevalence of opportunistic flora (St. aureus, Enterobacter, Citrobacter, Klebsiella, Proteus, Candida fungi) and a reduced level of the indigenous flora(Bifidobacteria, Lactobacteria, E. coli).By the end of the MP treatment, there was a statistically significant increase in the number of the indigenous flora in the children from the main group compared to the children from the control group.

Conclusion: A multi-strain probiotic can affect allergic inflammation in children with food allergy, which contributes to the effectiveness of the therapy.

TP1092 | Combination of pre- and probiotics as a new perspective in the treatment of lactose intolerance

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Background: Lactose intolerance is defined as a clinical syndrome characterized by pain, abdominal distention, flatulence, and diarrhoea following lactose consumption and affects approximately 75% of the world population. Specific probiotic strains have been proposed for the management of lactose intolerance, particular those with a specific β-galactosidase enzymatic activity. The aim of this observational study was to investigate the efficacy of a symbiotic combination of lactic acid bacteria and inulin in patients with lactose intolerance.

Method: 38 adult subjects with physician-diagnosed lactose intolerance received a symbiotic combination of *Bifidobacterium lactis* W51, *Lactobacillus acidophilus* W22, *Lactobacillus plantarum* W21, *Lactococcus lactis* W19 and inulin for 6 months. Symptom reduction was assessed using the SQLM (symptom questionnaire for lactose malabsorption) and changes in lactose consumption were analyzed. Secondary evaluations involved the changes in the proportion of patients with a positive hydrogen breath test (HBT).

Results: Symptoms of lactose intolerance were significantly decreased after 3 and 6 months of the symbiotic administration compared to baseline measurement. After 3 months, 71% of lactose intolerance patients reported an improvement of their symptoms, 66% patients after 6 months of administration. The proportion of patients with a negative HBT increased compared to baseline measurements: 0% at baseline, 65% after 3 months, and 81% after 6 months of administration.

Conclusion: These results show that the symbiotic supplementation *Bifidobacterium lactis* W51, *Lactobacillus acidophilus* W22, *Lactobacillus plantarum* W21, *Lactococcus lactis* W19 and inulin can improve the symptoms of patients with lactose intolerance and open new perspectives in the use of specific symbiotics in the treatment of lactose intolerance.

TP1093 | Comparison of different dietary instruction Methods for children with suspected or mild hen's egg allergy

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Background: To compare the safety and efficacy of different dietary instruction methods to discontinue egg elimination in patients with mild hen's egg allergy.

Method: We performed an oral food challenge (OFC, T1) using 2 g of boiled egg white in patients of 1-4 years of age who were positive for egg white IgE and ovomucoid-IgE < 3.5 kUA/L. Patients were either naïve in egg consumption or had a history of immediate, but non-anaphylactic allergic reaction to hen's egg. After a negative OFC result, patients were randomly assigned to the Step-up Oral Food challenge Test (SOFT) or home increment groups. The SOFT group started eating 2 g of boiled egg white at least 4 times per week at home, and repeated step-up OFCs with a single dose of 5, 10, and 20 g every 5-8 weeks. The home increment group started eating 2 g of egg white at least 4 times per week, and increased the dose 20% at home every week when they successfully consumed the instructed dose. Patients in both groups visited an outpatient clinic every 5-8 weeks to undergo an OFC or follow-up examination (T2, T3, T4). The primary outcome was the proportion of patients who tolerated 20 g of boiled egg white at the final visit (T5) 4-6 weeks after T4. We also evaluated the frequency of dose-related adverse events and parents' anxiety based on a self-reported questionnaire. This trial is registered in the University Hospital Medical Information Network Clinical Trials Registry (UMIN 000024192).

Results: Between September 2016 and July 2018, we randomly allocated 55 patients to the SOFT (n = 33 [60%]) and home increment (n = 22 [40%]) groups, and analyzed 46 patients. Eight patients were excluded because they were lost to follow-up or based on the parent's decision. One patient discontinued the study after a moderate adverse reaction of multiple urticaria after the first 2 g of intake at home. At T5, the proportion of patients who tolerated 20 g of egg white was 30/31 (96.8%) in the SOFT group vs 10/15 (66.7%) in the home increment group ($P = 0.01$). No serious adverse reactions were observed in either group. Parents' anxiety, as measured by the total score of State-Trait Anxiety Inventory (STAI), did not differ between the groups.

Conclusion: The SOFT method was more effective than home increment as a dietary instruction to discontinue the elimination of hen's egg in patients with mild hen's egg allergy.

TP1094 | Assessment of potential cross-reactivity with tree nuts, peanut and seeds in Japanese children with macadamia nut allergy

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Background: Macadamia nut (*Macadamia tetrraphylla and Macadamia integrifolia*) is consumed in the world. The epidemiological studies in the US have shown that food allergy to macadamia nut is not rare. However, few clinical cases of allergy to macadamia nut have been documented. In addition, cross-reactivity with other foods in macadamia nut remains to be investigated. In this study, we aimed to assess the cross-reactivity of macadamia nut with other tree nuts, peanut and seeds in Japanese children with macadamia nut allergy.

Method: Protein extracts of macadamia nut, peanut, almond, cashew, walnut, hazelnut, pistachio, pine nut, sesame, and buckwheat were prepared using optimized buffers. For assessment of the cross-reactivity of macadamia nut, the protein extracts were applied for inhibition ELISA using sera of six patients (age 2 to 6 years-old). These patients received of the doctor's diagnosis of macadamia nut allergy at Tokyo Metropolitan Children's Medical Center. Three of them had history of anaphylactic reaction after ingesting macadamia nut. Our study was approved by the independent review board of the Tokyo Metropolitan Children's Medical Center (H28-57b), and we obtained informed consent from the patients' caregivers.

Results: The ELISA inhibition assay showed that IgE-reactivities to macadamia nut were inhibited in a dose dependent manner when protein extracts of walnut and hazelnut were pre-incubated with the sera from allergic subjects without anaphylaxis. However, there was almost no inhibition by any protein extract of examined other tree nuts, peanut, and seeds, when those were pre-incubated with the sera from the three subjects with anaphylaxis.

Conclusion: Anaphylaxis could be developed by allergens without cross-reactivity in macadamia nut allergy. In contrast, walnut and hazelnut allergy, which could be developed through the cross-reactivity, should be carefully examined among children with mild allergic symptoms to macadamia nut.

TP1095 | Wheat-dependent exercise-induced anaphylaxis: Clinical presentations and management in a UK adult cohort

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Background: Wheat-dependent exercise-induced anaphylaxis (WDEIA) occurs when wheat ingestion is accompanied by exercise, with or without other co-factors. The wheat proteins w5-gliadin and high molecular weight (HMW) wheat glutenins are reported to be the major allergens involved. The aim was to investigate symptoms, co-factors and levels of specific IgE (spIgE) to wheat and w5-gliadin found in our patient population diagnosed with WDEIA.

Method: We collected data by retrospectively searching the electronic clinical record system using the terms WDEIA and FDEIA. Data were analysed using Excel.

Results: 19 patients (15 male, 4 Female) were identified with a positive clinical history and evidence of sensitisation to w5-gliadin or wheat and were included in the study. Mean age: 51 years; range 20-70 years; age range of highest prevalence 41-50 years. Seven patients had allergic-comorbidities; the most common being allergic rhinitis (4) and asthma (3). The most common presenting symptom was rash, followed by angioedema and dyspnoea. One patient had testing originally in New Zealand, so results were not on our database. Of the remaining 18 patients, 13 were tested to wheat. 62% had a negative SPT and 50% had a negative spIgE to wheat. One patient had elevated spIgE to wheat only; whereas the remainder were all sensitised to w5-gliadin. 2/19 patients had non-steroidal anti-inflammatory agents identified as cofactors in addition to exercise. 18/19 patients were prescribed adrenaline and one managed their symptoms with anti-histamines only. The majority (50%) of patients opted for full wheat avoidance with the remainder avoiding wheat 2-4 hours before or after exercise.

Conclusion: In our cohort of patients, WDEIA was most prevalent in males and in the 41-50 age group. Most patients had no allergic-comorbidities and had negative SPT and /or negative spIgE to wheat. Once diagnosed, most patients with WDEIA opt for total wheat avoidance.

TP1096 | Knowledge and proficiency of dietitians regarding food allergy in Lebanon

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Background: Food allergy (FA) is a public health issue with increasing prevalence worldwide. So far, there is no treatment for FA. Its Management relies on avoidance diets and treatment of symptoms in case of an allergic reaction. Knowledge of dietitians in the diagnosis

and management of FA is crucial for disease management. Tackling FAs and its management by dietitians have shown persisting gaps in their knowledge and stressed the need to evaluate this aspect

Method: An anonymous questionnaire of 35 questions was posted online via Qualtrics®. The link was sent to dietitians listed on the website of the syndicate of dietitians as well as to members of the Lebanese Academy for Nutrition and Dietetics (LAND). Also the link to the questionnaire was posted on private groups of Lebanese dietitians as well as sent to personal contacts.

Results: 95 participants answered the questionnaire. Lebanese dietitians rated themselves as being highly competent in different areas of FA management: understanding the definition of FA involving the immune system (43.16%), developing/implementing avoidance diets for children and adults (50%), educating patients and families on food avoidance (label reading and cross-contact) (67.02%), meeting the dietary needs of children/adults with multiple food allergies (46.81%) and evaluating safe foods in schools or hospital (39.36%). This self-reported high competency seems to have major gaps in regard to FA. Eighty four percent stated that FA can be severe but not fatale, 73% consider that anaphylactic shock resolves directly after treatment, 46% don't know that epinephrine can be injected through clothing and 97% think that precautionary labeling is required by law.

Conclusion: This study is the first to tackle knowledge and proficiency of dietitians regarding food allergy in Lebanon. It revealed the need amongst Lebanese dietitians to increase their knowledge regarding various fields of food allergy: diagnosis management and patient education. Increasing their knowledge on how to develop food challenge tests, to manage feeding problems, to administer self-injectable epinephrine will have a tremendous impact on the quality of life of allergic patients.

TP1097 | The importance of interaction in nutritional counselling

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Background: The diagnosis of food intolerances is a major challenge for nutritionists. In order to diagnose intolerances, special allergological knowledge is required. Technology has the potential to make nutritional counselling more efficient. In order to explore this potential, the BMBF (German Federal Ministry of Education and Research) founded project "DiDiER: Digitized services in nutritional counselling" added newly developed technical components to the still predominantly paper-based nutritional counselling. The aim of DiDiER is to improve the quality of a nutrition consultation by supporting the consultants in their work with electronically based workflows and analysis. However, nutrition consultation can't be reduced to a pure information and knowledge exchange. In addition to a professional expertise, soft skills such as empathy and a collaborative style of communication are of major importance, as the patient is not a pure consumer, but is actively involved as a "co-producer" in the creation of the service. Thus, the interaction itself becomes a central element and contributes to the quality of the consultation. The evaluation of the newly developed components therefore always takes place with regard to its effects on interaction.

Method: The importance of interaction for the quality of nutritional counselling was investigated through observational participation in counselling sessions and the conduct of several expert interviews.

Results: The interaction has a decisive influence on the patient's compliance. Good compliance is the result of successful communication between the dietician and the patient. Therefore, a patient-centred, dialogical way of working and active listening play a central role in nutritional counselling. The collection of "soft facts" and the identification of psychosocial needs leads to an individual consultation strategy for each patient. Social interaction, however, is not a competence that can be isolated, but is interconnected with the professional expertise of the consultant.

Conclusion: Nutrition counselling is a deeply analogous process that opposes a complete digitalisation. Technology can support human labour but never completely replace it, especially in nutrition counselling, which lives to a large extent from the social and communicative abilities of the counsellor. Technology should therefore be used in such a way that it supports the interaction between consultant and patient and does not obstruct it.

TP1098 | Welcoming Patients With Food Allergy: What Is The Preparation Of Schools And Restaurants?

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Background: Food allergy is a growing public health concern problem and an increasing number of allergic reactions begin to occur in the community, in places such as schools and restaurants. This study aimed to evaluate the perceptions of professionals in the education and catering sectors regarding the preparation of schools and restaurants to welcome food-allergic patients.

Method: 50 professionals from the education sector and 30 professionals from the catering sector, recruited from the participants of the FAC Program (Food Allergy Community Program), were included in this study. The perceived schools' preparation and food-allergic students 'difficulties were addressed, through 10 questions to be answered with five-point Likert-type scale. The good work practices of the restaurants in order to welcome and safely serve food-allergic clients were addressed through 20 *yes/no/I don't know*

questions. The tools were self-administered and were available online on the FAC program page on the University of Porto e-learning platform. Statistical analysis was performed using SPSS Statistics ® 22.0 and included descriptive analyses (proportions).

Results: For schools, 70% of school staff have already dealt with food-allergic students but only 46% considered that their school is prepared to welcome food-allergic students. Additionally, less than 40% believed that food-allergic children can easily relate to peers and less than 30% found it easy to dine at school. 100% agree that school staff should have more knowledge about food allergy and emergency situations.

For restaurants, more than 60% of the participants reported the existence on of indications on cross-contact prevention, allergens on the menu and updated technical datasheets in the establishment but only 13.3% have an emergency plan. Additionally, 56.7% received training in food allergy, but only 43.3% are trained in food-labeling reading and interpretation.

Conclusion: The experiences and perceptions of professionals in both sectors shown that there is a need for more training targeting specific food allergy management related to communication, education, service, and emergencies. The results also reinforce that community awareness for behavior change and increased health literacy is crucial for a safer inclusion of the food-allergic patient.

TP1099 | Intervention for management and control of food allergens in school canteens in Hortaleza district 2014-2017 in Madrid, Spain

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Background: The observed increase of food allergy in the population, especially in children in recent decades, highlights the need for progress in improving all factors related to the prevention of food allergy events at school. The aim of this study was to determine the level of management and control of food allergens in school canteens in Hortaleza District, Madrid (Spain) after an intervention that included information, training and a control program regarding the handling of allergen-free diets for children with a diagnosis of food allergy according to a specialist report.

Method: A survey that included 27 schools in Hortaleza District (all self-catering), was carried out in 2014 and repeated in 2017, after implementing measures related to food safety information, training, and control with the participation of school staff, families and children. From a total of 1378 served meals, 72 were food allergen-free ones. Information about self-implemented preventive measures regarding consideration of food allergens as a potential hazard, the existence of the specific written program, the identification system (menu/cooking utensils), scheduled processing, the existence of specific tables in the dining room for these children and health and support staff, were collected in a Hazard Analysis Critical Control Point (HACCP) checklist.

Results: Pre and post intervention HACCP checklist compliant were: 63%/88% schools considered food allergens as a risk, 51%/81% had a written prevention program, 63%/90% had a description of food allergen-free diets' preparation, 33%/33% had a specific area for food processing and 30%/30% had identified utensils/equipment for preparation. 52%/52% compliant storage of raw materials which guarantee the non-occurrence of cross contamination. 37%/37% cooked the food allergen-free diets before other meals. For packaging and identification, 59%/67% had sealed containers, 51%/67% had identified places in the dining room for these children and 74%/67% had a specific monitor. 37%/41% had health staff. There were recorded thirteen and three food allergic reactions respectively during this period.

Conclusion: The percentage of compliant items on the HACCP checklist increased after the intervention. We believe that the application of the food allergy control program at school canteens in this District, could have contributed to the lower number of allergic events observed in 2017. This aspect of food security should be stablished to prevent food allergy events at schools.

TP1100 | Presenting features and management of infant anaphylaxis

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Background: Anaphylaxis is a severe, life-threatening, systemic hypersensitivity reaction, which can occur at any age. Data on childhood anaphylaxis are limited and even less information is available on infant anaphylaxis, an area of intense interest especially since the early food introduction guidelines were put into place.

Method: We performed a retrospective case-note review over the period of 1 year (between January-December 2016) for infants presenting with anaphylaxis at Texas Children's Hospital. The aim of our study was to examine causes, clinical features and severity of infant anaphylaxis.

Results: We identified 15 infants among a total of 275 children presenting with anaphylaxis over a 1-year period. Median age was 8 months (range: 4-11 months). Food was the most common cause of anaphylaxis (73%) with egg the predominant trigger (53%), followed by milk (7%), peanut (7%) and banana (7%). Drugs were responsible for 20% of episodes, with antibiotics the most common medication trigger identified. All infants presented with cutaneous symptoms, followed by respiratory (60%), gastrointestinal (53%), and other (7%). Urticaria was the predominant skin symptom, followed by wheeze as the most common respiratory symptom and vomiting (predominant gastrointestinal symptom).Onset of symptoms was fast (within 15 minutes) in the majority (67%), whereas in 7% of cases symptoms developed after 30 minutes. Management included administration

of antihistamines, epinephrine and steroids in most. Almost all infants (87%) received epinephrine as rescue treatment, as per international guidelines. Three infants (20%) required 2 or more doses.

Conclusion: Infant anaphylaxis is most commonly due to a food trigger, with egg being the most frequent. In the majority, symptoms occur soon after ingestion. Cutaneous symptoms were a universal finding in our cohort, followed by respiratory and gastrointestinal symptoms. We identified severe anaphylaxis in 20% of infants, requiring multiple doses of epinephrine administration prior to resolution. Education on the use of emergency medication and management of allergic reactions is crucial, for both parents and healthcare professionals.

TP1101 | Factors predicting anaphylaxis in children with tree nut allergies

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Background: Tree nut (TN) allergies are the most common cause of fatal anaphylaxis and generally ongoing food allergies throughout life.

Method: We aimed to investigate the predicting factors for TNs anaphylaxis in children. For this purpose, whole study population were divided into two groups as patients with anaphylaxis (n = 90) and patients with reactions other than anaphylaxis (n = 94). Children with TN allergies were evaluated for the predictors of anaphylaxis by using multivariate logistic regression analysis.

Results: A total of 184 TN allergic children 4.9 (3.2-6.9) years were included in the study. Of these, 90 experienced anaphylactic type of reaction upon exposure to at least one type of TNs. In the study group, the highest frequencies of anaphylaxis occurred with hazelnut (40%), pistachio (38.8%), cashew nut (27.7%), and the least common TN anaphylaxis was seen with almond (2.2%). SPT (P = 0.006) and sIgE (P < 0.001) measurements with causative TNs, total IgE (P = 0.011) and serum basal tryptase (sBT) levels (P < 0.001) were significantly higher in patients with anaphylactic reactions compared to patients with non-anaphylactic reactions. Patients with anaphylactic reactions to any TNs had increased frequency of asthma (14.4% vs 7.4%, P = 0.008) and egg white allergy (65.6% vs 30.9%, P < 0.001) compared to patients with non-anaphylactic reactions, respectively. In multivariate analysis, female gender [OR: 4.905, 95% CI: 1.266-19.001, P = 0.021], sBT levels [OR: 2.287, 95% CI: 1.431-3.654, P < 0.001], concomitant egg white allergy [OR: 4.135, 95% CI: 1.016-16.481, P = 0.048] and concomitant asthma [OR: 3.874, 95% CI: 1.109-13.526, P = 0.034] were risk factors for anaphylaxis. The optimal cut-off value for sBT was 2.06 ng/mL, with a sensitivity of

	Presence of anaphylaxis (n = 90)	Presence of non-anaphylactic reactions (n = 94)	*P* value
Current age (years)*	5.6 (3.6-7.3)	4.5 (3-6.2)	0.031
Gender (M/F)	56/33	71/24	0. 080
Onset age of TNs symptoms (months)*	10.0 (6.0-13.5)	12.0 (6.0-17.5)	0.577
Age of serum basal tryptase measurement (months)*	40.0 (25.5-61.2)	29.0 (19.5-56.0)	0.251
sIgE kU/L *	8.2 (2.0-26.1)	1.9 (0.7-6.5)	<0.001
SPT mm*	5.50 (3.5-9.5)	8.00 (5.5-11.1)	0.006
Total IgE kU/L*	258.0 (117.5-773.5)	158.5 (41.6-412.7)	0.011
Serum basal tryptase level (ng/mL)*	3.8 (2.6-5.2)	1.6 (1.0-2.7)	<0.001
Eosinophil count (/mm3)*	400 (200-600)	400 (200-700)	0.665
Basophil count (/mm3)*	0 (0-100)	0 (0-100)	0.559
Presence of allergic diseases			
Allergic rhinitis (n/%)	14 (14.4%)	7 (7.4%)	0.128
Atopic dermatitis (n%)	68 (75.6%)	60 (63.8%)	0.085
Asthma (n/%)	40 (44.4%)	24 (25.5%)	0.007
Pollen sensitization (n/%)	16 (17.8%)	10 (10.6%)	0.252
Family history of atopy (n/%)	25 (27.8%)	29 (30.9%)	0.801
Concomitant allergy with			
Peanut (n/%)	7 (7.8%)	13 (13.8%)	0.189
Cow's milk (n/%)	23 (25.6%)	29 (30.9%)	0.426
Egg white (n/%)	59 (65.6%)	29 (30.9%)	<0.001
Positive OFC at least one TNs (n/%)	28 (31.1%)	4 (4.2%)	0.354

85.9% and a specificity of 69%, as well as an area under the curve (AUC) of 0.810 ($P < 0.001$, 95% CI 0.717– 0.903). sBT levels of 1.94 ng/mL and 5.30 ng/mL predicted clinical reactivity at 50% and 95% probabilities.

Conclusion: Different aspects, including gender, higher mast cell load/activation and stronger atopic background such as coexisting egg allergy, asthma contribute to the development of anaphylactic reactions to TNs in children.

TP1102 | Life: In a nut free shell

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Background: Food allergy is a global concern increasing in prevalence in westernised countries. In the UK it is estimated that 5-8% of children have a food allergy. Peanut allergy commonly presents in the first five years of life with 80% often persisting into adulthood. Currently there is no cure therefore avoidance remains key part of management.

Method: UK wide survey by the patient charity Allergy UK captured data on children aged 2-11 years with diagnosed peanut allergy focussing on quality of life issues. parents/carers completed the survey online. Questionnaire comprising of two demographic questions, 13 clinical questions, including diagnosis method, symptomatology of the allergic reaction and 2 questions about expectations for new treatments disseminated using Allergy UK's social media channels via survey monkey platform. Questionnaires analysed using Survey Monkey's data analysis functionality. 'Filter' and 'compare' functions used to uncover correlations between different variables.

Results: 1441 participants started the questionnaire with 1079 participants completing and included in analysis.

59% of participants were male and 41% female. Symptoms of severe allergic reaction were reported more often in children aged between 9 and 11 years old.

22% of children aged 10 years old collapsed in comparison with only 5% of children aged 2 years old.

13% of children aged 11 years old reported symptoms of angioedema including the face, lips and tongue compared to 4.5% of 2-year olds.

100% of parents whose children attended A&E 10 times or more due to peanut allergy believed it is possible to react to inhaled peanut protein. This decreased to 25% for parents of children who had visited A&E between one and four times.

For 99% of participants, avoidance was highlighted as key in their management plan. Expectations of treatment were influenced by the severity of the allergic reaction; the weighted score given to a treatment that protects against accidental reactions increased from an overall 10.96 to 11.24 when only responses from parents/carers whose children collapsed were considered.

Conclusion: Perceptions about risks and satisfaction with management plans were associated with the severity of previous allergic reactions. Initiatives and therapies which reduce the likelihood of reactions from accidental exposure could have a positive impact on the quality of life for children and families. Advances in science and research bring hope and treatment choice to those with peanut allergy.

TP1103 | "People don't know how severe some of them can be": An exploration of beliefs and attitudes in adolescents with food allergy

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Background: Adolescents with food allergy (FA) are in an age group that is associated with higher rates of allergic and fatal allergic reactions due to increased risk-taking behaviour. In this study we aimed to explore attitudes and beliefs of adolescents aged 11-16 years with food allergy to better understand adolescents with this condition.

Method: Qualitative design using semi-structured interviews.

Results: Four themes were drawn from the data: 1) "I think everyone would take it more seriously." - Nut allergies as more serious than other food allergies, 2) "I don't like talking about the needle, it just scares me." – Adrenaline auto-injectors and needle anxiety, 3) "They're like annoying don't get me wrong but they're not like super life threatening." - How severity of FA symptoms affects beliefs. 4) "I would like to have been born with it and grown up with it because then I would have understood it more and I wouldn't be so worried." Challenges of recent diagnosis.

Adolescents had varying beliefs dependent on age, gender, food they were allergic to, severity of FA and age of diagnosis.

Conclusion: Peer support was seen as extremely important and should be incorporated into the development of interventions designed to help adolescents manage their food allergy safely. Beliefs around the seriousness of different allergens and beliefs associated with the age of diagnosis warrant further investigation.

TP1104 | Health related quality of life among adolescents with food hypersensitivity

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Background: Food hypersensitivity often debut in childhood and may persist into adolescence. Adolescence is a vulnerable period in

life with physical, physiological and social changes. These changes may be further complicated when adolescents also live with food hypersensitivity. There is sparse of information about health related quality of life in relation to food hypersensitivity among adolescents. The aim of this study is to examine self-reported health related quality of life in association with food hypersensitivity among adolescents from a Swedish population-based prospective study.

Method: This study was conducted within the birth cohort BAMSE, where children were recruited from the general population and followed up to adolescence. In a follow up at 16 years information about food hypersensitivity and health related quality of life were obtained (n = 2730). Food hypersensitivity was defined as parental-reported specific symptom(s) to a specific food(s) the past 12 months. Health related quality of life was self-reported by the adolescent using the generic instrument EQ-5D that involved the descriptive systems (investigated in five dimensions) and the visual analogue scale, EQ VAS.

Results: In total, 22.6% fulfilled the definition of food hypersensitivity. Adolescents with food hypersensitivity reported more problems in the EQ dimension pain or discomfort (24.0% vs 17.1%, $P < 0.001$) and in the dimension anxiety or depression (26.9% vs 21.4%, $P = 0.004$) compared to those without food hypersensitivity. Adolescents with food hypersensitivity also had a significant lower EQ VAS compared to those without food hypersensitivity (median 89 vs 90, $P = 0.004$).

Conclusion: In our population-based birth cohort, food hypersensitivity is associated with impaired health related quality of life in adolescence. Future studies should aim to investigate how different phenotypes of food hypersensitivity influence health related quality of life in adolescence.

TP1105 | Qualitative exploration of the adult's perspective of undergoing a food challenge test

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Background: Very limited research has been carried out on the experience of undergoing a food challenge test in adults. The aims of this study were to gain an understanding of the patients' experience, feelings and views of undergoing a food challenge test and the impact of this test on their health-related quality of life.

Method: Semi-structured interviews of adults who had undergone a food challenge test for diagnosis or to confirm tolerance to a suspect food were conducted. Thematic analysis was used to allow for an in-depth understanding of the views, beliefs and experiences of affected individuals. Data analysis was assisted by NVivo qualitative data analysis software.

Results: Twenty-four participants with a mean age of 35.21 yrs +/- 7.07 were included in this study. All participants found undergoing a challenge test an overall positive experience irrespective of whether the outcome was positive i.e. they had a reaction or negative (allergy excluded). There was consensus among the participants that the food challenge test made a significant difference to their lives. Key themes identified as leading to improved quality of life were 1) clarity about what they are or not allergic to, 2) relief to know cause of symptoms or that they can eat the food tested 3) confidence and reassurance to retry if the test was negative and if positive, reassurance that their suspicions were confirmed. Individuals who tested negative, found 4) food re-introduction and improved diet beneficial. The food challenge led to 5) improved social life especially being able to take part in social activities including eating out and travelling and had a 6) positive impact on family and relationships.

Conclusion: Prior to having the food challenge, participants lived in fear and uncertainty. They were following very restricted diets impacting on their social lives and relationships with others. Following the challenge, their quality of life markedly improved with many describing this as a transformation. The findings of this study support the need for more widespread provision of food challenge testing in adults.

TP1106 | Post traumatic stress disorder (PTSD) in parents of pediatric anaphylaxis patients; using BDI-II, BAI, And IES-R

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Background: Anaphylaxis is a life-threatening disorder. Having a child with anaphylaxis can have a significant long-term psychological impact on parents and this anxiety may in some cases be transferred from parents onto their children. The aim of this study was to investigate the post traumatic stress disorder (PTSD) in parents of pediatric anaphylaxis patients.

Method: To investigate the PTSD for parents of child with anaphylaxis, we had been using the Korean Beck Depression Inventory II (BDI-II), Korean Beck Anxiety Inventory (BAI), and of Impact of Event Scale-Revised Korean version (IES-R-K) scale in 13 hospitals

between Oct. 1, 2016 and Sep. 30, 2018. Written informed consent was obtained from all participants after they were fully informed of the details of the study.

Results: Total 217 parents who had children having experienced anaphylaxis, were participated in this study. Response rate of BDI-II was 99%, mean score was 14.07 (S.D.; 11.03), 37.0% was scored 17 or above (depression), and Cronbach's alpha was 0.939. Response rate of BAI was 96%, mean score was 13.09 (S.D.; 11.04), 18.8% was scored 22 or above (anxiety), and Cronbach's alpha was 0.969. Response rate of IES-R was 90%, mean score was 27.36 (S.D.; 17.28), 54.4% was scored 25 or above (impact), and Cronbach's alpha was 0.963.

Conclusion: We found that 37.0% (BDI-II), 18.8% (BAI), and 54.4% (IES-R) of all parents who had experienced a traumatic event were classified as having a high risk of PTSD, and this proportion is higher than that of other groups (e.g., firefighters). This finding indicates that PTSD-related interventions and management are needed for parents of children with anaphylaxis.

TP1107 | Nine-year survey of anaphylaxis in an allergy department

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Background: Aim: To characterize patients with anaphylaxis in an allergy outpatient department, allowing a better understanding regarding etiology, clinical manifestations and management.

Method: Retrospective analysis of voluntary notified anaphylaxis by our allergists' staff during a nine years period (January 2010 to December 2018). Clinical presentation, etiology, allergic history and management disease were evaluated.

Results: 508 patients had history of anaphylaxis, with mean age 29.2 ± 19.7 years, being 57% females. 26% were children (≤10 years), 12% teenagers (11 to ≤ 19 years) and 62% adults (≥ 20 years). The majority had an allergic personal history (83%), 35% had asthma. The median age of the first anaphylaxis episode was 23 years (1 month-82 years). In 39 children, the first episode occurred in first year of life. The majority had food-induced anaphylaxis (FIA) (52%): nuts (n = 57), cow's milk (CM, n = 52), shellfish (n = 52), fresh fruits (n = 41), peanut (n = 27), egg (n = 21), seeds (n = 17), fish (n = 11) and wheat (n = 4). In the children/teenagers group, the main foods implicated were: CM (n = 49), nuts (n = 36), egg (n = 21), fresh fruits (n = 17) and peanut (n = 16). In the adults group were: shellfish (n = 42), fresh fruits (n = 24), nuts (n = 21) and seeds (n = 13). Drug-induced anaphylaxis (DIA) occurred in 35%: nonsteroidal anti-inflammatory (n = 72), beta-lactam antibiotics (n = 69), anesthetic agents (n = 12) and proton pump inhibitors (n = 8). The remaining anaphylaxis causes were food-dependent exercise-induced (n = 19), cold (n = 17), hymenoptera sting (n = 14), latex exposure (n = 4) and others (specific immunotherapy (n = 3), horse exposure (n = 1), anisakis (n = 1)). There were 9 cases of idiopathic anaphylaxis. Patients reported mostly mucocutaneous (97%) and respiratory symptoms (79%), followed by cardiovascular (34%), gastrointestinal (32%), glottis edema (28%) and loss of consciousness (15%). The majority (79%) started symptoms within 30 minutes after trigger exposure. 81% were admitted to emergency department, although only 33% were treated with adrenaline. 26% had anaphylaxis recurrence (74 patients had ≥ 3 episodes).

Conclusion: In our population, FIA was the main trigger of anaphylaxis, followed by DIA, physical agents and hymenoptera sting. Adrenaline was underused, as previously reported by others. We stress the importance of systematic anaphylaxis notification and improvement of educational programmes in order to achieve a better preventive and therapeutic management of this potentially life-threatening entity.

TP1108 | Understanding the health and economic benefits of commercial peanut immunotherapy products: A cost-effectiveness analysis

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Background: Commercial epicutaneous peanut immunotherapy (EPIT) and peanut oral immunotherapy (POIT) may offer significant quality of life improvements for patients with peanut allergy, but the cost-effectiveness of commercial peanut immunotherapies is uncharacterized. We therefore sought to evaluate critical inputs affecting the cost-effectiveness of commercial EPIT and POIT.

Method: Microsimulations (n = 10 000 per treatment strategy) with Markov modeling were performed evaluating four-year old children over an 80 year time horizon. The base-case costs incorporated a caregiver-reported willingness to pay threshold of $3839 for safe and effective food allergy treatment. Predictive biomarkers or oral challenges were incorporated after the first year of therapy with additional analyses of immunotherapy risk reduction of severe accidental reactions and probability of sustained unresponsiveness (SU) to peanut after four years. Rates of therapy-associated adverse reactions and quality of life improvements associated with changes in eliciting/tolerated peanut doses were modeled along with quality-adjusted life years (QALY), anaphylaxis, therapy-associated anaphylaxis, and fatalities.

Results: In the base-case, EPIT cost less than POIT ($154 662 SD, $46 716 vs $163 524,SD $56 800), had fewer total episodes of anaphylaxis (1.33, SD 1.55 vs 3.83, SD 5.02), and therapy-associated

anaphylaxis (0.62, SD 1.30 vs 3.10, SD 4.94), but lower QALY accumulation (26.932, SD 2.241 vs 26.945, SD 2.320). The incremental cost-effectiveness ratio (ICER) for EPIT was $216 061 and for POIT was $255 431. Models were sensitive to therapy cost, health state utility, risk reduction of severe accidental reactions, and SU rates. At 7% improvement in health state utility, both therapies were cost-effective with value-based pricing of $6568 (EPIT) and $5235 (POIT). If very high rates of SU can be achieved in longer-term models, EPIT and POIT could produce savings in terms of both cost and QALY.

Conclusion: Commercial EPIT and POIT may be cost-effective under some assumptions. Further research is needed to understand the degree of health state utility improvement associated with each therapy, degree of protection against severe allergic reactions, and rates of SU.

MONDAY, 3 JUNE 2019
TPS 28
MECHANISMS OF FOOD ALLERGY

TP1109 | Does Foxp3 methylation affect the development of food allergy in children?

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Background: Food allergy is a multifactorial disease that affects the pediatric population, with a global incidence of 8%. Genetic as well as epigenetic factors play an important role in its development. In particular, T-regulatory cells have a leading position in maintaining immune tolerance. These cells are divided into subpopulations with $CD4^+$ $CD25^+$ being the most important in immune regulation. T-regulatory cells express the transcription factor FOXP3, which is a molecular marker in peripheral blood. Furthermore, recent studies have shown that lower levels of FOXP3 expression are associated with the development of atopic conditions, including food allergy in children. The purpose of this study is to investigate the methylation pattern of specific CG nucleotides located upstream of the FOXP3 gene in children with food allergy and in non-allergic children.

Method: The study population consisted of 18 children. The food allergy diagnosis based on clinical criteria, skin prick tests and specific IgEs (ImmunoCap). After an extensive search of the literature there were specific GC dinucleotides of the FOXP3 gene selected, evolutionarily conserved between human and mouse and their methylation levels seem to regulate its expression. In addition, for the isolation of the total peripheral blood mononuclear cells (PBMCs) venous blood was exacted from the children. To determine and quantitate the methylation/demethylation levels of each individual CpG site along the DNA sequence, the Pyrosequencing CpG assay was used. The statistical analysis of the results was carried out with the SPSS v20 program.

Results: There was no statistically significant difference in the methylation pattern of CG dinucleotides in the PBMCs of children with food allergies compared to non-allergic children ($P = 0.755$).

Conclusion: The isolation of cellular populations from peripheral blood leads to a heterogeneous cell mixture. Moreover, the epigenetic phenomena do not appear with the same extent in all cell types of a tissue. The methylation analysis in the subpopulation of T-regulatory cells ($CD4^+$, $CD25^+$) which express specifically the intracellular transcription factor FOXP3 is a priority in the following research plans.

TP1110 | Investigation of increased prevalence of IgE specific for galactose alpha-1,3-galactose in patients with coronary artery disease

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Background: A recent survey of 260 patients presenting with self-reported allergy to red meat identified 249 cases who had IgE specific for galactose alpha-1,3-galactose (alpha-gal). Of these patients 60% had presented at age 40 years or older and 80% reported that their reactions started 2 hours or more after eating red meat or other mammalian derived food. While the detailed mechanism for the delay is not established the foods consumed are predominately mammalian tissues that have been associated with Coronary Artery Disease (CAD). The logical explanation of the delay is that it reflects the absorption and digestion of glycolipids down to the size of LDL, i.e. 20 nm or less. Lipid particles of this size are generally considered to be a significant contributor to the inflammation in arteriosclerotic plaques.

Method: We investigated the relevance of IgE to alpha-gal to the characteristics of arteriosclerosis in 118 subjects who underwent medically indicated coronary artery catheterization including Intra Vascular Ultrasound (IVUS).

Results: Out of the subjects studied 26% had positive IgE to alpha-gal. Among the IgE positive subjects there was an increase in atheroma burden; among the 79 subjects ≤ 65 years old this increase was highly significant ($P < 0.001$). Using IVUS the characteristics of the Atherosclerotic plaques were also shown to have significantly increased fibrofatty, necrotic and calcified features. By contrast there was no association between atheroma burden and IgE specific for either inhalant or peanut allergens ($P = 0.38$ and 0.26 respectively).

Conclusion: Our recent data suggest that α-gal is a dominant cause of red meat allergy in central Virginia and also that among adults in this region sensitization to α-gal was strongly associated with CAD. Our evidence does not explain the mechanism; however, it is consistent with a model where specific IgE could target an epitope present on lipid particles such as LDL which are thought to be a major factor in severity of CAD. In addition our results suggest that this CAD risk may relate to eating foods such as dairy products even in patients who not aware of allergic symptoms after eating yogurt, butter, milk or cheese.

TP1111 | Novel insights into the allergenic relationship between red meat and bovine milk

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Background: Red meat allergy is a severe form of food allergy with delayed symptoms including anaphylaxis where the IgE antibodies are directed against a carbohydrate epitope, galactose-α-1,3-galactose (α-Gal). Many red meat allergic patients report allergic symptoms upon consumption of milk or dairy products. The aim of the project was to investigate the allergenic relationship between bovine milk and red meat at a molecular level.

Method: Adults with diagnosed red meat allergy (n = 27) were recruited and their specific IgE levels to α-Gal, beef and milk were analyzed by ImmunoCAP. Milk proteins were assayed by immunoblot and inhibition ELISA for the presence of the α-Gal epitope and for the binding to red meat allergic patients' IgE. The involvement of the carbohydrate epitope in the IgE binding to milk proteins was assessed by an inhibition assay with thyroglobulin. Basophil activation test was performed with milk and milk proteins in samples from 11 red meat allergic patients and 2 controls.

Results: All patients were IgE positive to milk, but the IgE levels to milk were lower than those to α-Gal or beef. Significant correlations between IgE levels to milk and α-Gal (r_s = 0.64, P < 0.01), as well as between milk and beef (r_s = 0.90, P < 0.01) were observed. Immunoblot analysis of milk proteins revealed bovine γ-globulin (BGG) as α-Gal carrier. Other milk proteins, α-lactalbumin, β-lactoglobulin, α-casein, β-casein and κ-casein were negative for the presence of α-Gal epitope. BGG was also shown to bind IgE antibodies of red meat allergic patients. Inhibition immunoblot with thyroglobulin resulted in the loss of IgE binding to BGG. Additionally, ELISA experiments showed that BGG, as well as whey proteins exert a dose-dependent inhibition of red meat allergic patients' IgE binding to α-Gal. Inhibition with raw milk and commercially available milk preparations showed that raw milk exerted a slightly higher inhibition of the IgE binding to the α-Gal epitope than the commercially available milks. Importantly, activation of red meat allergic patient's basophils by BGG and milk was demonstrated.

Conclusion: BGG was identified as a major milk carrier of the α-Gal epitope that bound IgE antibodies and furthermore activated basophils of red meat allergic patients. This study highlights the importance of milk as allergenic food source among the meat allergic population.

TP1112 | Household exposure to food allergens: A risk for sensitization?

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Background: Exposure to food allergens is a pre-requisite to the development of food allergy. It is not fully understood what levels of exposure to allergens or what route of exposure is most important for allergic sensitization. Food allergens present within household dust and in the air may contribute to allergic sensitization of individuals at risk of developing food allergies. We sought to determine the precise levels of specific food allergens within household dust, and measure levels inhaled exposure using an innovative nasal filter.

Method: To determine which allergens were present, settled dust samples were collected from a range of households within Europe. Seven common allergens were simultaneously quantified using a highly sensitive multiplex array for allergens; peanut (Arah3 and Arah6), milk (Bosd5), egg (Gald2), hazelnut (Cora9), cashew (Anao3) and shrimp (tropomyosin). To determine whether aerosolized food allergens could be detected using the nasal filter method, they were worn in a variety of settings and compared to the standard IOM method using PTFE filters.

Results: Each of the allergens assessed were readily found within household dust. Major allergens from egg (Gald2) and milk (Bosd5) were found to be the most abundant, with levels as high as 275 μg allergen/gram dust. The least abundant food allergen was Cora9. All seven allergens were also detected using the nasal filter method. This novel approach to air sampling proved to be more effective as, for every allergen, a higher fraction of samples were positive and detected at higher levels in comparison to the standard IOM method.

Conclusion: Food allergens within household dust are within the same range and higher as those known to cause sensitization to common indoor allergens. Milk and egg are especially prominent exposures. These findings suggest that household dust may be an important source of food allergen sensitization. Additionally, levels of aerosolised food allergen could also be detected and suggest sensitization could occur through inhalation.

TP1113 | The role of chitinase 3-like–1 in the regulation of food allergy

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Background: Food allergy is an increasing health problem that has no approved treatment. Chitinase 3-like–1 (Chi3 l1) is a type of

chitinase-like proteins that lacks chitinase activity. Chi3 l1 is highly expressed in a variety of cells, including macrophages, neutrophils, epithelial cells. Also, it is known to be associated with cancer and type 2 inflammation. However, the role of Chi3 l1 in food allergy has not been investigated.

Method: IgE-mediated food allergy was induced in BALB/c female mice by sensitization and challenge with ovalbumin (OVA). Symptoms of food allergy were defined as clinical and diarrhea scores and a change in body temperature. We then analyzed serum levels of IgE, Th2 cytokines (IL-4, 5, 13) mRNA expressions and histopathologic investigations.

Results: Clinical and diarrhea scores were increased and core temperature was decreased in OVA induced food allergy mouse model. Chi3 l1 mRNA and protein expression levels were elevated in OVA challenged WT mice. Also, serum IgE, Th2 cytokines mRNA levels, histological injury scores and disruption of junctional complexes were increased in OVA-challenged WT mice compared to the control mice. In OVA-challenged Chi3 l1 knockout mice, those levels were lower than OVA-challenged WT mice. Moreover, we showed that M2 macrophage makers (CD 206, Ym 1/2, Arginase 1) were elevated in OVA-induced WT mice and they were attenuated in OVA-induced Chi3 l1 knockout mice.

Conclusion: Our observations suggest that chi3 l1 plays an important role in Th2 inflammation of food allergy. And chi3 l1 deficiency may alleviate food allergy symptoms.

TP1114 | Measurement of naturally occurring variation in allergens and isoforms of peanut

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Background: Food allergen extracts used for diagnosis/treatment of allergies are evaluated by measuring relevant allergens to ensure consistent results. Biological indicators are difficult, expensive and typically produce variable results. Molecular characterization of allergens using techniques such as mass spectrometry (MS) are preferable. Peanut contains multiple proteins thought to be most responsible for allergic reactions. Recent release of the peanut genome allows accurate description of the genes encoding peanut allergens for the first time, including isoforms. This study describes a workflow for the accurate quantitation of peanut allergen families and isoforms thereof, and describes the variation across cultivars.

Method: 20 samples of different cultivars of common peanut market types were extracted, reduced, alkylated, digested, and subjected to data-dependent MS analysis. Label-free quantitation of allergens was performed using a custom list of peptides derived from the peanut genome to represent allergen protein families, and different peptides to uniquely quantify allergen isoforms.

Results: It is possible to measure the composition of peanut allergens using quantitative analysis of specific peptides using peptides selected based on the genome and detection. The total content of the major allergens, Ara h 1, 2, 3, 6 and 7 were relatively consistent (<20% CV) in peanut cultivars. Minor allergens (Ara h 8, 9, 10/11) showed greater variability. However, certain individual isoforms of Ara h 3, showed considerable (>50 fold) variation, but other Ara h 3 isoforms compensated for the differences.

Conclusion: Quantitative analysis of ten major allergenic protein families required the measurement of 98 peptides and is within the capabilities of modern LC-MS-MS. Based on the presence of many non-abundant allergen forms, and on the low variability observed, such detailed measurement is unlikely to be needed for routine analysis of clinical materials. Variation was largely limited to low-abundance allergens of doubtful clinical significance. We suggest that quantitative molecular data such as that presented may be used to describe allergen variation in clinical materials. We also suggest that genetic and environmental variation of major allergen content is sufficiently low that significant differences in efficacy are unlikely. Standardization of MS methods for allergen quantitation would greatly simplify introduction of clinical materials for allergen diagnostic and therapeutic use.

TP1115 | Metabolomic analysis of an allergic enteritis murine model by GC-MS

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Background: Allergic diseases are on the rise, and food allergies are one of the most prevalent and concerning. From these, allergic enteritis (AE) – the inflammation of the small intestine caused by food allergy – is gathering increasing interest. Concerning allergic mechanisms, allergen-specific IgE is one of the proven effectors of allergy, although food-allergic phenotypes that are independent of IgE also exist. Moreover, metabolomics is a new science that seeks altered metabolic changes in living organisms. Thus, the aim of this work is to shed light on the molecular mechanisms of AE, specifically the role of IgE, by means of metabolome analysis using an animal model.

Method: To induce AE, wild-type (WT) mice and IgE knock-in (IgEki) mice expressing IgE instead of IgG were used. These were sensitized with ovalbumin (OVA, an egg white allergen) and challenged with a diet containing egg whites. Control mice received egg white diet without OVA sensitization. From these mice, whole faeces and serum samples were extracted and used for metabolomic analysis by

Gas Chromatography coupled to Mass Spectrometry (GC-MS). GC-MS is a technique that allows the detection of volatile compounds or those that are volatile after derivatization, such as TCA intermediates, fatty acids, phenolic compounds, and amino acids, among others. Significant compounds were obtained for all the comparisons between the four groups.

Results: Metabolic profiles of serum and total faeces were characterized, obtaining 91 metabolites for serum and 265 for faeces. From these, after a statistical analysis, 129 compounds were found to be significative for faeces and 15 for serum, in total for all comparisons. The comparisons with the highest number of compounds were between the most extreme groups ("allergic IgEki *vs* non-allergic WT" & "allergic WT *vs* non-allergic IgEki"). IgEki mice displayed more severe symptoms and their metabolic signatures were significantly different from WT mice. It is also notable that the high levels of IgE have an impact on the metabolome as well as the allergic condition.

Conclusion: We have analysed the metabolome of a murine model of AE. It appears that the metabolic changes of AE are affected by IgE levels, which suggests a role of IgE in the pathology. Further studies for the validation of these results and the identification of a metabolomic signature associated with AE development would advance in the search for the molecular mechanism of AE and biomarkers for allergic conditions.

TP1116 | Germ-free mice do not develop food allergy despite high levels of sensitization due to mast cells impaired functionality and gut homing

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Background: Mucosal mast cells (MC) are key players in IgE-mediated food allergy (FA). We tested the hypothesis that commensal bacteria are essential for MC migration to the gut and their maturation impacting the susceptibility to FA.

Method: The development and severity of FA was studied in germ-free mice (GF), conventionalized germ-free mice, conventional mice (CV) and mice mono-colonized by *L. plantarum* WCFS1. Mice were sensitized *i.p.* by ovalbumin (OVA group) or PBS (CTRL group) together with Alu-Gel-S adjuvant on Day 1 and 14. Two weeks after the second *i.p.* sensitization, mice were challenged 8 times at 2-3 day intervals (days 28-44) by *i.g.* gavages of OVA or PBS. Diarrhea occurrence was monitored after each *i.g.* exposure and temperature was measured after the last *i.g.* exposure. Total and OVA-specific antibodies, MC protease-1, IL-4 and IL-13 in sera and jejunal homogenates were determined by ELISA. We focused on mast cells analysis: a) presence and numbers in jejunum by staining of jejunal histologic sections; b) number and maturation degree in peritoneal lavage by flow cytometry; c) functionality - GF and CV mice were challenged by injection of degranulation compound 48/80; d) mRNA expression of MC homing receptor *Cxcr2* and its ligands by RT-PCR.

Results: Systemic sensitization and oral challenge of GF mice with OVA led to increased level of specific IgE in sera compared to CV mice. Remarkably, despite the high level of sensitization, GF mice did not develop diarrhea or anaphylactic hypothermia. In the gut, GF mice expressed low levels of the MC tissue-homing markers and harbored fewer MC which exhibited lower level of MC protease-1 after challenge. Additionally, MC in GF mice were less mature as confirmed by flow-cytometry and reduced edema formation after injection of degranulation-provoking compound 48/80. Co-housing of GF mice with CV mice fully restored their susceptibility to develop FA. However, this did not occur when GF mice were mono-colonized with *L. plantarum* WCFS1.

Conclusion: Our results demonstrate that microbiota-induced maturation and gut-homing of MC is a critical step for the development of symptoms of experimental FA. This new mechanistic insight into microbiota-MC-FA axis can be exploited in the prevention and treatment of FA in humans.

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TP1117 | Characterization of circulating dendritic cells in peanut allergy patients

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Background: The prevalence of peanut allergy (PA) has increased worldwide reaching 1.1% in developed countries. PA often causes anaphylaxis with potential life risk, and unfortunately it has no standardized safe treatment except the avoidance of peanut consumption. Dendritic cells (DCs) initiate and modulate the adaptive immune response. In food allergies, when exposed to a food, DCs capture and present food allergens to TCD4 + helper (Th) cells, inducing Th2 responses.

Objective: To characterize the immunophenotype of DCs obtained from patients with PA.

Method: We performed a cross-sectional study in 18 patients with PA and 6 non-atopic subjects. The inclusion criteria were a compatible history of PA and demonstration of specific IgE to peanut by prick test and/or specific IgE. PBMCs from peripheral blood were obtained by Ficoll gradient. Myeloid DCs (mDCs) and plasmacytoid DCs (pDCs) were differentiated using $CD11c^{+}CD123^{-}$ and $CD11c^{-}CD123^{+}$, as surface markers, respectively. Expression of HLA-DR, CD40, CD86, CD1c, FcεRI and surface-bound IgE were evaluated on DCs by flow cytometry.

Results: Subjects' age was 18 ± 14.4 years and 50% were women. 95% of the PA patients had an atopic comorbidity, 25% allergic rhinitis, 37% atopic dermatitis and 29% asthma. PA patients had higher number of circulating DCs than non-atopic controls (354 ± 185 cells/μL vs 148 ± 154 cells/μL, $P = 0.018$). The populations of mDCs and pDCs showed a higher expression of surface-bound IgE in PA vs controls ($P < 0.05$ and $P < 0.01$ respectively). In addition, myeloid DCs showed an increase in the expression of CD1c, CD86 and FcεRI ($P < 0.05$).

Conclusion: DCs from PA patients had an activated immunophenotype and higher expression of FcεRI and surface-bound IgE, providing evidence that circulating DCs actively participate in the allergic response in these patients.

TP1118 | Potential role of CD73 in basophil non-reactivity

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Background: Basophils can interact with other immune cells to inhibit or enhance cells' function during inflammation. The basophils from 10% to 20% of healthy donors fail to upregulate surface activation markers that correlate with histamine release in response to FceRI cross-linking. Since these non-responder basophils express normal surface FceRIa subunit, it has been proposed that there are differences in the intracellular signaling pathways. When basophil activation test is utilized to assess clinical food allergies, the results from non-responder patients are regarded as false negatives. Non-responder basophils seem to be donor-specific since the results can be reproduced from the same donor over different time points. We asked whether the converse is true: Can other immune cells impact basophil function to lead to non-responsiveness?

Method: We assayed peripheral blood of 45 peanut allergy patients, 37 of which were undergoing peanut oral immunotherapy (OIT), for CD20 + CD73-CD71 + CD25 + B regulatory cells.

Results: Even though there was no correlation between B-regulatory cells and the degree of CD63 and CD203c upregulation of basophils, we found a statistically significant negative correlation between CD20 + CD73 + B cells ($P < 0.02$) and CD3 + CD73 + T cells ($P < 0.04$) with the basophil activation markers induced by anti-IgE. There were no differences in these markers among non-allergic controls, peanut allergic patients, and peanut OIT patients. Clinical reaction to peanut in patients with non-responder basophils were limited to the skin, presenting with hives. As an additional control to assess basophil reactivity, we chose eosinophilic esophagitis where the underlying mechanism is not immediate type 1 hypersensitivity. Patients with eosinophilic esophagitis (n = 11) had a much higher percentage of non-reactive basophils (55%) compared to our peanut allergy cohort.

Conclusion: These findings collectively suggest a CD73 mediated regulatory mechanism that controls immediate type allergic reactions. CD73 is an ecto-5'-nucleotidase that converts AMP into adenosine. Adenosine, at physiologic concentrations, inhibits in vitro IgE-mediated human basophil histamine release in a dose-dependent fashion and is paralleled by an adenosine-induced increase in cAMP levels. The inability of basophils to respond to stimulation through high affinity IgE receptor may play a protective role in preventing food-induced allergic reactions from progressing into full anaphylaxis.

TP1119 | Allergen-specific profiling of sera from patients with peanut allergy

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Background: Peanut allergy is one of the most common food allergies causing potentially deadly IgE-mediated hypersensitivity reactions such as anaphylaxis and asthma. Peanut-allergic patients also have high titres of potentially protective IgG antibodies, with the IgE-IgG balance most likely determining whether the patient develop symptoms or not. To date, 16 different peanut allergens have been identified and among them, Ara h 1, Ara h 2, Ara h 3, and Ara h 6 are known to bind IgE in the majority of peanut-allergic patients. Ara h 2 and Ara h 6 have been shown to cause more severe IgE-mediated reactions than Ara h 1 and Ara h 3, indicating that certain allergens are more prone to elicit an anaphylactic shock.

Method: Sera from 95 peanut allergic patients were tested for reactivity against five different peanut allergens, Ara h 1, Ara h 2, Ara h 3, Ara h 6, and Ara h 8, by an in-house sandwich ELISA method and by coating plates with the different major allergens. Serial titrations of the sera were added, and after detection with biotinylated anti-human IgG, individual titres were determined.

Results: All tested sera were positive for Ara h 3. Against Ara h 1, 92 sera (97%) had detectable IgG. Ninety sera (95%) were reactive with Ara h 2, while 88 (93%) and 78 (83%) sera were reactive against Ara h 6 and Ara h 8, respectively. When comparing the titres, we observed high IgG titres against the allergens Ara h 1, Ara h 2, and Ara h 3, while lower IgG titres were detected against Ara h 6 and Ara h 8.

Conclusion: All patients had detectable allergen-specific IgG but they showed different reactivity against distinct peanut allergens. Differences in the serology of peanut allergic patients may reflect a peculiar clinical history, for which reason the serological titres will be correlated with allergen-neutralisation tests by competition ELISA and leukotriene release from basophils.

TP1120 | Epitope-specific antibody profiling in food allergy using novel multiplex immunoassay: Design and validation

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Background: Identification of allergenic IgE epitopes is instrumental for the advancement of diagnostic and prognostic tests for food allergy. We've developed a novel Bead-Based Epitope Assay (BBEA) to screen multiple epitopes in a large number of samples. In this work, we've proposed a quantification and validation pipeline, characterizing the assays reproducibility and comparing its performance to peptide microarrays (MIA).

Method: 66 milk and 50 peanut epitopes were uniquely coupled to beads and incubated in 96-well microplates with plasma from 47 milk- and 281 peanut-allergic patients, developed with a secondary antibody to IgE or IgG4, and the median fluorescence intensity (MFI) was quantified with a Luminex-200 reader. MFI was normalized and converted to epitope-specific antibody binding (ESAB) values. To asses reliability and reproducibility, 8 samples of peanut reactivity levels were processed in triplicates in 3 independent laboratories and assessed with intra-class correlation coefficients (ICC). To compare BBEA with MIA the same experiment was repeated across two days for each assay.

Results: ESAB values were not affected by microplate well position or reading order, but there was a detectable batch effect indicative of individual microplate runs that could be corrected by using linear modeling. ESAB values had "excellent" within laboratory reliability across replicates with ICC > 0.9 and > 0.75 for IgE and IgG4. Across laboratories, most of the ESAB variance was attributed to the sample type and not the laboratory (99% vs 0.3% for IgE), with ICC > 0.8 across all epitopes. BBEA was moderately correlated with MIA (r = 0.27, P = 0.028), but the effect size was almost 3 times higher in BBEA, with 98% epitopes detected compared with a 30% detection rate by MIA. Lastly, we examined the potential of epitopes as biomarkers of allergy severity. A classification tree predicting oral food challenge outcome identified intermediate values of IgE where IgG4 levels showed a protective effect that is absent at very high or low IgE values.

Conclusion: We have developed a BBEA protocol, quantification and quality control pipeline that allows unbiased detection of antibody binding to sequential allergenic epitopes. BBEA is reliable, reproducible and more sensitive than current MIA technology. BBEA allows rapid quantification of ESAB in a large number of samples, providing a new tool for diagnosis, prognosis and endotype discovery in food allergy.

TP1121 | Effect of housing conditions and route of administration in inducing peanut allergy in mice

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Background: Previous studies have reported that specific housing conditions of mice can either inhibit or exaggerate the induced disease response because of the macro-environment of the holding facility. In addition, the route of sensitization plays a significant role in inducing food allergy. The aim of this study was to investigate the effect of housing conditions on manifestation of food allergy in Balb/c mice using intraperitoneal and oral induction routes.

Method: 5 groups (n = 6) of female Balb/c mice 6-8 weeks old were maintained in a specific-pathogen-free (SPF) facility as well as a conventional facility for two weeks after weaning. Mice were subsequently sensitised with peanut extract in PBS using two different routes, oral and intraperitoneal. Alum (intraperitoneal) and Cholera toxin (oral) were used as adjuvants in this study. Three sensitisations and two challenges were performed at one-week interval. Clinical symptoms were scored, and temperature recorded after the last challenge. Cytokine analysis was performed in supernatant collected from activated splenocytes.

Results: No significant weight changes were observed in either facility. However, the allergy scores were significantly different between the facilities. Peanut specific IgG and IgG1 antibody levels were significantly increased in the alum induced peanut allergy group in both SPF and conventional facility. Peanut specific IgG2a however demonstrated increased levels in the conventional facility only. Importantly, a significant decrease in body temperature was detected in the conventional facility after both challenges, in contrast to the SPF facility. Increased levels of IL-4, IL-5 and IL-13 expression was observed in supernatant of activated splenocytes from the SPF facility in allergy induced groups.

Conclusion: This study indicates that changes in housing condition of experimental mice can significantly affects the induction of food allergy depending on route of induction. Further analysis pertaining to microbiome and mesenteric lymph node cells can provide more insights into underlying mechanism and changes in cell subsets involved in this process.

TP1122 | Investigation of the sensitization potential of sunflower seed proteins in a mouse model

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Background: World population is growing and demand in food proteins is constantly increasing. We then need to identify new sustainable protein sources. Plant proteins are an interesting alternative for animal proteins because of their lower environmental impact. Sunflower seeds (SFS) are rich in proteins and are already consumed in some countries. Few cases of food allergic reactions have been reported and they have been attributed mostly to the nsLTP Hel a 3 and the 2S-albumin SFA-8. Here, we aimed to investigate the allergenic potential of SFS proteins using a mouse model of allergic sensitization.

Method: Different fractions from SFS whole extract were prepared by using selective precipitation and separation through a combination of chromatographic methods. SFS proteins were characterized by 1D- and 2D-gel electrophoresis and by mass-spectrometry. Their potential of sensitization was then investigated in BALB/c mice orally sensitized to a SFS whole protein extract, using cholera toxin as adjuvant. Humoral and cellular responses to SFS proteins were analyzed by measuring IgG1 and IgE responses in sera and by performing ex vivo splenocyte reactivation. Cross-reactivity between SFS and peanut proteins was also investigated in mice orally sensitized to peanut.

Results: Several 2S albumins and LTPs, including SFA-8 and Hel a 3, were isolated from sunflower seed. In the mouse model, we observed that the IgE responses induced in SFS-sensitized mice were not restricted to SFA-8 and Hel a 3, as evidenced by the IgE-reactivity of other 2S-albumins and LTP. Humoral and cellular responses to SFS proteins in peanut-sensitized mice were very weak, thus suggesting a relatively low level of cross-reactivity between SFS and peanut proteins.

Conclusion: The mouse model of oral sensitization to SFS protein allowed us to identify potentially new allergenic proteins, belonging to known allergen families. The IgE-reactivity of the corresponding identified and purified proteins will be now evaluated using sera from SFS- and peanut-allergic patients.

TP1123 | Hydrolyzed faba bean proteins prevent the development of allergic reaction in a mouse model of cow's milk allergy

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Background: Food allergy is an IgE-mediated disease whose incidence has increased during the last decade, especially in young children. Currently the only efficient solution offered to patients is food restriction. Thus, infant formulas with extensively hydrolyzed proteins are used for children with a cow's milk allergy (CMA). However, some babies do not tolerate these formulas either. The aim of this study was to investigate the tolerance of an infant formula with hydrolyzed faba bean proteins in a mouse model of CMA.

Method: BALB/c mice were sensitized by two intraperitoneal (i.p.) injections of cow's milk proteins adsorbed on aluminium hydroxide. Unsensitized control mice received i.p. of saline and aluminium hydroxide. At day 26, sensitized mice were orally challenged with either cow's milk proteins or faba bean hydrolysate whereas unsensitized mice received water (n = 10 per group). The clinical symptoms in animals were evaluated by anaphylactic scores (a scoring system based on observations of scratching, ruffled hair, reduced activity and abnormal breathing). Animals were sacrificed 24 h after the challenge. Total and specific-IgE and mMCP-1 levels were quantified in serum.

Results: Both sensitized mice groups presented similar high levels of total and specific IgE which is the demonstration of effective sensitization in both groups. Control mice did not present allergic reaction and have low levels of mMCP1. All milk-challenged mice presented allergic reactions (puffy eyes, scratching, ruffled hair, reduced activity with or without increased respiratory rate). This was associated with high levels of mMCP1. By contrast, faba bean hydrolysate-challenged mice did not present any allergic reaction and their seric levels of mMCP1 were not significantly different from those of the control mice.

Conclusion: Consumption of faba bean hydrolysate prevented the development of anaphylactic reactions in cow's milk allergic mice.

TP1124 | Method for quantitation of food allergens in serum by basophil histamine release

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Background: To develop a method quantitating food allergens in serum by measuring histamine release from passively sensitized basophils, elicited by allergen in serum, after oral intake of the food in

question. The method is based on a model utilizing calculations of Area Under Curve (AUC), plotted against LOG transformed allergen

Method: Blood bank buffy coat basophils were stripped off IgE and passively sensitized using sera containing high IgE titer against the allergen in question. Basophils were incubated with a known allergen standard and the unknown allergen preparations in 12 dilutions. Residual cellular histamine was measured by the glass fiber method and results expressed as per cent histamine release. Area under titration curves of allergen standards were calculated and plotted against logarithmically transformed allergen concentrations resulting in a linear dose-response curve. This standard curve was used to calculate allergen levels in unknown samples based on AUC.

Results: Samples of buffer and serum were spiked with peanut in concentrations ranging between 500 and 2.5 pg. peanut/mL showed recoveries ranging from 88% to 102% with CV's ranging from 3.5% to 31%. Recoveries were independent of peanut concentration but CV % increased when peanut levels decreased. These data were reproduced using other allergens like pork kidney (Gal-Alpha-Gal), hazelnut, grass and wasp. Sensitivity, recovery and variability were dependent on 1) high tittered specific IgE in serum (80 to 100 kIU/l), highly responding basophils (> 30% histamine release to anti-IgE) and well-defined food allergen standard containing documented amounts of all individual allergens.

Conclusion: Food allergens can be detected in buffer and serum in the pg/mL level and the method can be used to determine allergen kinetics after food intake, determine the fraction of food uptake in relation to intake and determine allergen content in food matrices.

TP1125 | A jurkat based NFκB-EGFP INKT reporter cell line to evaluate the interaction of food-derived lipids with INKT cell receptors

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Background: Invariant natural killer T (iNKT) cells recognize lipid antigens presented by the class I MHC homolog CD1d and thus get activated. Upon activation iNKT cells secrete Th1, Th2 and Th17-type cytokines, and have been identified as important players in different types of immune responses. However, their role in food allergic reactions is still not understood. In parallel, the potential immunogenic role of lipids present in allergenic foods has been discussed during the sensitization and elicitation phase. In order to address these questions a reporter cell line was established to screen potential ligands and their activation capacity.

Method: An iNKT reporter system was engineered by introducing the human iNKT TCR into a human leukemic Jurkat T cell line carrying an NF-kB-driven fluorescent transcriptional reporter construct (JE6-1$^{REP\text{-}iNKT}$). Additionally, to remove CD1d expression from JE6-1$^{REP\text{-}iNKT}$ cell surface and block possibility of antigen self-presentation, we generated a β2 microglobulin knock cell line (JE6-1$^{REP\text{-}iNKT\text{-}\beta2M_KO}$) using the CRISPR/Cas9 method. BW^{STIM}, a human CD1d transfected thymoma cell line, was generated and used as antigen presenting cells. Reporter induction (NF-kB-driven eGFP-expression) was measured by flow cytometry. The specificity and sensitivity of our system was compared to IL-2 production by murine DN32.D3 iNKT cell hybridomas, following activation by a-Galactosylceramide (a-GalCer)-loaded CD1d molecules, and co-culture assays utilizing BW^{STIM} and CD1d transfected murine fibroblasts (L-CD1d) cell lines. Functional activity of JE6-1$^{REP\text{-}iNKT\text{-}\beta2M_KO}$ cells was tested additionally with two commercially available a-GalCer derivatives - OCH and 7DW8-5, respectively.

Results: JE6-1$^{REP\text{-}iNKT}$ cells stably expressing the human iNKT TCR were shown to specifically react with iNKT antigens presented via CD1d. The detection limit for α-GalCer was equivalent for JE6-1$^{REP\text{-}iNKT}$ and DN32.D3 cell lines.

Conclusion: JE6-1$^{REP\text{-}iNKT}$ reporter cell line is a useful tool to study the capacity of food derived lipid antigens to activate human iNKT TCR. Applying the present iNKT reporter cell system as a high throughput screening tool could help to identify lipid candidates relevant for allergenicity. In addition, our reporter system is remarkably faster and more cost-effective, compared to traditional assays.

TP1126 | Interaction of mustard Seed 2s albumin allergen Sin a 1 with intestinal epithelial cells as a model in allergy development

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Background: Mustard is a widely consumed spice, often appearing as a hidden allergen in foods and triggering unexpected symptoms. Sin a 1, a 2S albumin, is the major allergen from mustard seeds but little is known about its sensitization pathway and its ability to interact with the intestinal epithelium. Previous studies showed that Sin a 1 is able to bind acid phospholipid vesicles, suggesting its ability to interact with cell membranes. The aim of this experimental work was to assess the intrinsic ability of Sin a 1 to interact with intestinal

epithelial cells *in vitro*, altering the integrity of the epithelial barrier and thus contributing to allergic sensitization.

Method: The purification of Sin a 1 from mustard seeds protein extract was performed using chromatographic methods. HT-29 cells were grown to confluence in 48 wells-plates and exposed for 24 h to different concentrations of Sin a 1, mustard seed extract or LPS and afterwards supernatants were collected. Caco-2 cells were grown in 12 well transwell-plates till 2-3 weeks post-confluence (TEER values were up to 500 $\Omega.cm^2$), and apically exposed to different concentrations of Sin a 1, mustard extract or saline buffer (Sin a 1 isolation buffer) during 24 h. TEER was measured, basolateral supernatants were collected, 4 kDa FITC-dextran permeability was determined and cell viability was assessed (WST-1).

Results: Sin a 1 dose-dependently increased the secretion of CCL20 ($P < 0.05$) by HT-29 cells and showed a similar pattern for IL-33 without affecting cell viability. On the other hand, the highest amount of Sin a 1 strongly reduced TEER of Caco-2 cells ($P < 0.001$), whereas enhanced FITC-dextran permeability ($P < 0.01$). However, only the mustard extract increased CCL20 ($P < 0.01$) and IL-33 ($P < 0.05$) secretion by Caco-2 cells. Caco-2 cell viability was not affected by the purified allergen nor the extract.

Conclusion: Mustard seed extract or Sin a 1, the major allergen from mustard seed, enhanced the release of allergy-associated mediators by IEC depending on the cell line used and Sin a 1 showed the intrinsic capacity to break epithelial barrier integrity. Sin a 1 may therefore have sensitizing properties via its interaction with the intestinal epithelium. More studies are required to corroborate the obtained results and to further elucidate the accurate mechanisms of action.

TP1127 | Expression of prostaglandin E2 receptors in food anaphylaxis

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Background: Preliminary data of our group has shown that prostaglandin E2 (PGE2) decreases IgE-mediated basophil activation in both food-induced NSAIDs-dependent and NSAIDs-independent anaphylaxis, in an *in vitro* model of basophil activation test. PGE2 binds 4 different receptors with anti-inflammatory (EP2, EP4) and pro-inflammatory (EP3) activities. Our hypothesis is that food anaphylaxis patients have a altered PGE2 production and/or a PGE2 receptor expression profile that favors pro-inflammatory responses. Our objective was to compare PGE2 serum levels and the expression in basophils of COX metabolism-related genes (COX1, COX2, PGE2 receptors 1 (EP1), 2 (EP2), 3 (EP3), 4 (EP4)) of patients with food anaphylaxis.

Method: Patients with lipid transfer protein (LTP)-induced NSAIDs-dependent (group A N = 13) and NSAIDs-independent anaphylaxis (group B N = 18) and healthy individuals (HV, N = 18) were evaluated. All samples were obtained in baseline conditions (absence of allergic reaction). PGE2 levels (pg/mL) were measured by ELISA in serum samples at two time points (T0 and 60 minutes (T60) after blood drawn). Basophils were isolated by negative selection (Basophil Enrichment kit, StemCell) in leukocyte-rich plasma prepared from peripheral blood (HetaSep, StemCell). Gene expression was measured in isolated basophils by quantitative real-time PCR analysis and calculated by $2^{(-\Delta Ct)}$ method (ΔC_t = gene of interest-housekeeping gene). ELISA data are expressed as pg/mL PGE2 and gene expression as $2^{(-\Delta Ct)}$ mean±SD.

Results: No differences in serum PGE2 levels were observed at T0 (HV = 62.2 ± 32.6, A = 57.7 ± 23.9, B = 51.5 ± 16.4) and T60 (HV = 309.4 ± 257, A = 313.1 ± 183, B = 421 ± 274). An increase of PGE2 levels were observed at T60 compared to T0 in all groups, but with no significant differences between them. No differences were observed in the expression of COX1, COX2, EP1, EP2 and EP4. Only EP3 was upregulated in group B patients compared to HV HV = 0.52 ± 0.33, A = 0.6 ± 0.2, B = 0.65 ± 0.25, $P = 0.04$). The ratio $2^{(-\Delta Ct)}$ EP2/EP4 (HV = 0.24 ± 0.18, A = 0.31 ± 0.19, B = 0.35 ± 0.18, $P = 0.04$) and $2^{(-\Delta Ct)}$ EP3/EP4 (HV = 2.6 ± 2.9, A = 3.5 ± 2.9, B = 3.2 ± 1.3, $P = 0.02$) was also significantly higher in group B.

Conclusion: In the absence of allergenic stimulation, no apparent dysfunction of PGE2 production is observed in patients with food anaphylaxis regardless of cofactor involvement. However, LTP-induced NSAIDs-independent anaphylaxis patients may have PGE2 receptors expression profile that favors inflammation upon PGE2 binding.

MONDAY, 3 JUNE 2019
TPS 29
ALLERGENS, POLLUTANTS AND OTHER ENVIRONMENTAL FACTORS

TP1128 | Particulate matters downregulate the expression of structural components in normal human epidermal keratinocytes

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Background: The skin is exposed to environmental air pollutants such as polycyclic aromatic hydrocarbons (PAHs), volatile organic compounds (VOCs), and particulate matters (PMs). PM affects the progression of inflammatory skin diseases. Recently, it has been reported that the increased concentration of PM in ambient air is strongly related to progression of atopic dermatitis (AD) in children. Although exposure of the skin to PM has been associated with inflammatory or allergic skin condition, our knowledge regarding the effects on skin remains limited.

Method: PM2.5 samples were collected on quartz filters (37 mm, Pallflex). To obtain particles for *in vitro* exposures, filters were extracted using an ultrasound bath by replicating four 20 min cycles using sterilized water. Normal human epidermal keratinocytes (NHEK) was differentiated at the 80% confluent condition with 1.3 mM calcium chloride ($CaCl_2$) for 3 days. Following the differentiation, NHEK were exposed to 10 ug/mL of PM2.5 for 2, 6, and 24 hours. The mRNA expression of filaggrin (*FLG*), involucrin (*IVL*), loricrin (*LOR*), desmoglein 1 (*DSG1*), desmocollin 1 (*DSC1*), defensin beta 1 (*DEFB1*), 2 (*DEFB2*), 3 (*DEFB3*) and cathelicidin antimicrobial peptide (*CAMP*) was analyzed using quantitative real-time PCR.

Results: In NHEK, PM2.5 decreased the expression of genes encoding protein associated with permeability barrier formation (*FLG*, *IVL* and *LOR*), with desmosomal junction (*DSG1* and *DSC1*), and with tight junction barrier function (*DEFB3*) in a short-period time of exposure (for 2 hrs). However, PM2.5 did not affect the mRNA expression levels of other antimicrobial peptides, including *DEFB1*, *DEFB2* and *CAMP* in a differentiated NHEK.

Conclusion: Our results suggest that the PM exposure to the skin could cause the skin barrier dysfunction by downregulating epidermal structural components.

TP1129 | The effect of mechanical air purifier for improving allergic symptom scores of allergic children

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Background: The air quality and pollution in the air is completely dependent on the surroundings one lives in. capturing ourselves indoor during the high level of pollution also needs readdress as indoor air is usually dirtier than the air outdoors, due to trapping of air contaminants inside. Children as they are most likely to stay indoors for longer durations. This study aimed to evaluate the change of allergic symptoms from allergic children by using air purifier.

Method: 45 allergic children were recruited from Hanyang university Guri Hospital Pediatric Allergy Clinic (18 children with atopic dermatitis, 18 with allergic rhinitis, 9 with asthma). Samsung air purifier (Model No: AX90N9880, AX94N9980) was set up subject's family room and operated with filter-on for 28 days as acting day and filter-off for 28 days as control with average 14 hrs/day (8-24 hrs/day) since September 2018. Allergic symptom scores were self-checked on smart cellular phone by subjects' parents as Atopic dermatitis: SCORAD, allergic rhinitis: Total 4 nasal symptom score (T4NSS), Asthma: Asthma symptom score(ASS). At same period level of the PM10, PM2.5, pollens and NO_2, SO_2, O_3 were measured and recorded daily for air quality.

Results: Mean improved rate of SCORAD were 15.16%, T4NSS was 28.86%, ASS was 50.7% at on-filter of air purifier phase than at off-filter phase. There was no significant correlation between allergic symptom scores and the level of air pollutants and pollens in this period, but showed the lag-effect trend between them.

Conclusion: allergic symptom scores were improved by using mechanical air purifier set up in house of allergic children.

TP1130 | Association between prenatal exposure to PM2.5 and atopic eczema in Asian school-age children

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Background: Atopic eczema is a common inflammatory skin disease occurred in infants and children. Associations between ambient

particulate matter < 2.5 μm ($PM_{2.5}$) and allergic diseases have been suggested in previous epidemiologic studies. However, limited cohort studies have examined the role of prenatal exposure to $PM_{2.5}$ plays in the development of childhood eczema. We aimed to evaluate whether prenatal exposure to $PM_{2.5}$ was associated with eczema in a cohort of Asian school-age children.

Method: The study consists of 1169 full-term (≥37 weeks of gestation) school-aged children, part of the Longitudinal Investigation of Global Health in Taiwanese Schoolchildren (LIGHTS) cohort. Data related to clinical symptoms and physician-diagnosed eczema, and other pertinent demographic/ epidemiologic factors were collected using a modified International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire. Children with atopy were defined based on Phadiatop Infant test (≥ 0.35 PAU/L). Prenatal exposure to $PM_{2.5}$ levels were estimated by linking their residential addresses during prenatal stage to air quality monitoring stations operated by Taiwan Air Quality Monitoring Network (TAQMN). Multiple logistic regressions with covariates adjustment were carried out to examine the association of prenatal exposure to $PM_{2.5}$ with physician-diagnosed eczema.

Results: There were 426 (36.4%) children with physician-diagnosed eczema. The risk of physician-diagnosed eczema was increased with higher exposure to $PM_{2.5}$ during entire pregnancy (adjusted odds ratio (AOR) = 1.07, 95% confidence interval: 1.01-1.13). Particularly, higher exposure to $PM_{2.5}$ in the second trimester (AOR = 1.04, 95% CI: 1.01-1.08), but not first or third trimesters, significantly increased the risk of physician-diagnosed eczema. In addition, results from stratified analysis suggested that exposure to $PM_{2.5}$ during entire pregnancy was positively associated with physician-diagnosed eczema among children with atopy (AOR = 1.12, 95% CI:1.04-1.21), but not among those without atopy. In the second trimester, risk of physician-diagnosed eczema associated with PM2.5 among children with atopy (AOR = 1.05, 95% CI:1.01-1.09) was higher than those without atopy (AOR = 1.03, 95% CI:0.97-1.09).

Conclusion: This study shows that prenatal exposure to $PM_{2.5}$ was positively associated with atopic eczema in Asian school-age children.

TP1131 | Prenatal exposure to PM10 levels and development of childhood eczema

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Background: Previous studies have suggested that exposure to air pollution has increased the risk of developing childhood allergic diseases. However, the effect of prenatal exposure to particulate air pollutants, such as particulate matter with a diameter less than 10 μm (PM_{10}) on the risk of developing subsequent childhood eczema is unclear.

Method: In the present study, we included 1513 children born between 2010 and 2011 and participated in the Longitudinal Investigation of Global Health in Taiwanese Schoolchildren (LIGHTS) Cohort. We collected the demographic, epidemiologic and phenotype data using a modified International Study of *Asthma* and Allergies in Childhood (ISAAC) questionnaire. Prenatal exposure to PM_{10} during entire pregnancy and each trimester, respectively, was estimated based on the information provided by the Taiwan Air Quality Monitoring Network (TAQMN). We applied the ordinary kriging model coupled with land use regression model to assess the spatial-temporal variability of prenatal exposure to PM_{10}. We used multiple logistic regression analysis to estimate the association between exposure to PM_{10} and physician-diagnosed eczema with adjustments for potential confounders. We also performed stratified analysis by gender and atopy.

Results: Analyses included 1169 full-term children (mean age, 6.4 years). Overall, 36.4% of the children had physician-diagnosed eczema. An increased risk of physician-diagnosed eczema were significantly associated with exposure to PM_{10} during entire pregnancy (adjusted odds ratio (AOR) = 1.037, 95% confidence interval (CI) = (1.006-1.069)), while the association was significant only in the second trimester (AOR = 1.020, 95%CI = (1.004-1.036)) but not in the first or third trimesters. Stratified analyses showed that the association of second trimester exposure to PM_{10} with physician-diagnosed eczema existed only in boys (AOR = 1.029, 95%CI = (1.006-1.051)) and children with atopy (AOR = 1.021, 95%CI = (1.001-1.041), respectively.

Conclusion: Our results suggest a positive association between prenatal exposure to PM_{10}, especially in the second trimester, and the development of childhood eczema.

TP1132 | The effects of particulate matter exposure on allergic rhinitis-related hospital visits in the Republic of Korea

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Background: Although many epidemiologic studies have shown the association between particulate matter (PM) exposure and risks of allergic diseases, little have been examined for allergic rhinitis(AR) outpatient visits. The purpose of this study was to investigate the effects of PM exposure exceeding daily average environmental standards of Korea on all allergy rhinitis-related hospital visits.

Method: This was a population based case-crossover study using the National Health Insurance and air pollution data between January 1, 2014 and December 31, 2016. The event day was defined as the

day when PM exceeded daily average environmental standard. The control day was defined as the same day of the week before the event day.

Results: Compared with the control days, the average number of AR-related hospital visits on the 24-hr event days for PM_{10} were increased by 2.68%. The ratio of an average number of AR-related hospital visits increased from the 24-hr event day for PM_{10} to 4 days after the event day, peaking on the third day after the event day (1.109, 95% CI, 0.7141-1.7223).

Conclusion: We found a significant association between PM exposure exceeding the current daily average environmental standard and AR-related hospital visits. These results are expected to aid in establishing appropriate environmental standards and relevant policies for PM.

TP1133 | Urban particulate matter induces nasal epithelial barrier dysfunction by targeting tight junctions in human nasal epithelial cells

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Background: Exposure to airborne urban particulate matter (UPM) has been closely related to development and aggravation of respiratory disease, including sinonasal disorders. However, the influence of UPM on the nasal epithelial barrier and the underlying mechanism has not been investigated previously. The aim of this study is to investigate the effect of UPM on nasal epithelial tight junctions (TJs) and mucosal barrier function, and delineate these underlying mechanism.

Method: In this study, human RPMI 2650 cells and cultures of primary human nasal epithelial cells (HNECs) were exposed to particulate matter (PM_{10}) and fine particulate matter ($PM_{2.5}$). TJ and endoplasmic reticulum stress (ER stress) markers expression was measured using by real-time quantitative polymerase chain reaction, Western blot analysis and immunofluorescence. TJ integrity and nasal epithelial barrier function were evaluated by transepithelial electric resistance and paracellular flux. In addition, the effects of N-acetyl-L-cysteine (NAC) on UPM induced HNECs were investigated in vitro.

Results: Urban particulate matter significantly impaired the nasal epithelial barrier, as demonstrated by decreased mRNAs and protein expression of TJ markers in RPMI 2650 cells and cultures of human nasal epithelial cells. This was in parallel to reduced transepithelial electrical resistance and increased fluorescein isothiocyanate–dextran permeability. Pretreatment with NAC reduced the degree of UPM-mediated ER stress in HNECs and restored nasal epithelial barrier disruption.

Conclusion: These data suggested that particulate matter may induced nasal epithelial barrier dysfunction by targeting tight junction through the activation of ER stress in HNECs. Furthermore, disrupting this process with an inhibitor targeting ER stress responses could represent a novel promising therapeutic target in UPM induced sinonasal disease.

TP1134 | Air pollution is a risk factor for noncommunicable diseases in a small Brazilian city?

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Background: Air pollution has been associated with high prevalence of noncommunicable disease (NCDs), eg. cardiovascular and pulmonary diseases, in general population. Objective: To verify if air pollution was associated to NCDs in a small city in Brazil.

Method: Five hundred fifty-one patients, attended at three basic health units from Uruguaiana, Brazil, due to varied complaints, answered a questionnaire about outdoor and indoor air pollution exposure comparing people with NCDs [Arterial Hypertension /Chronic Respiratory Disease (AH/CRD)].

Results: Three hundred eighty two women (69%) were involved. Patients with AH/CRD use to work near to an air pollution source (18.1% vs 11%, $P = 0.02$), use to live near an air pollution source (45.6% vs 29.6%, $P = 0.0002$), mainly a street with high traffic vehicles (41.7 vs 33%, $P = 0.04$). There were no association between indoor air pollution and AH/CRD as seen active and passive smoking, respectively, (13.2% vs 12.4%, $P = 0.69$ and 26.9 vs 19.9%, $P = 0.06$).

Conclusion: Exposure to outdoor air pollution was associated to AH/CRD. Primary care physicians and health professionals should be guided on the harm of air pollution on people's health. Educational and protective measures should be urgently encouraged.

Keywords: pollution, primary care physicians, education, NCDs.

TP1136 | Efficacy of behavioural interventions for smoking cessation during pregnancy

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Background: Smoking during pregnancy is a significant risk factor both for women and their children. The monitoring of Russian general population (including Saratov city) during last decade demonstrated

that smoking is decreasing from 39.1% to 31.0% due to an increased awareness of the adverse effects and tightened tobacco legislation. However, smoking among women increased from 21.7% to 22.8% with a maximum of 35% (age 19-25 years). The negative effects of smoking during pregnancy can be significantly decreased by education programmes for smoking cessation.

Objective: This research aimed to evaluate the efficacy of collaborative special behavioral counseling for smoking cessation during pregnancy.

Method: The prevalence of smoking in fertile age women was monitored. 108 smoking pregnant women were recruited for special education programme (5R-Relevance-Risks-Rewards- Roadblocks-Repetition) in 3 urban clinics in 2016-2017. Initial health status, depression, smoking status (number of cigarettes smoked packs/years) were estimated. Fagerström Test, visual analogue scales and questionnaires were used to assess the nicotine addiction and motivation to quit smoking. CO testing of breath (1 ppm resolution) was also used, spirometry was performed in line with ERS/ATS standard. All these allowed to reliably measure the percentage of women with cessation as a result of education programme.

Results: Smoking among pregnancy women in 2016 was 10%. Nonpharmacological interventions (education programme) for promoting smoking cessation during pregnancy was effective in 48.15% (52 women quitted smoking), 51.85% - continued. The latter had a higher motivation to smoke (high Nicotine Dependence Scale – 28 women) and a lower motivation to quit. Positive effect was obtained with the help of guided self-education, including general and regional-specific materials about significant risk factors for women and their children, and references to smoke-free policies at home, work and public places.

Conclusion: Reducing smoking during pregnancy is a priority. The success of educational programmes can be significantly improved by identifying the patient's specific problems and unmet needs. Educational programmes and guided self-education can be implemented effectively in clinical practice, also acknowledging individual status of women and their specific issues.

TP1138 | The changes of sensitization rate to inhalant allergens over the last 10 years in Korea

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Background: The prevalence of sensitization to inhalant allergens can be changed due to alterations in outdoor environment or lifestyle. The climate change caused by global warming can affect pollen season and lifestyle trend in raising pets may influence dog or cat sensitization. The purpose of the study is to investigate the changes of sensitization rate to 6 common inhalant allergens during the last 10 years in a single tertiary hospital of Seoul, Korea.

Method: The 7635 cases with allergic diseases such as asthma, allergic rhinitis or atopic dermatitis underwent measurements of specific IgE to six common inhalant allergens (weed pollen, tree pollen, *D. farinae*, alternaria, cat dander and dog dander) using immunoCAP.

Results: The overall sensitization rate to 6 common aeroallergens increased from 14.9% in 2008 to 21.7% in 2017. The sensitization rate was significantly increased in 2017 compared to 2008 in tree pollen (4.8%->15.3%), weed pollen (3.6%->13.1%), cat dander (3.8%->14.1%) and dog dander (5.9%->13.6%). The rate of sensitization to alternaria and house dust mite also showed an increase in 2017 (10.1%, 48.2%, respectively) compared to 2008 (5.8%, 37.9%, respectively), but there was no statistical significance. The monthly prevalence of sensitization to tree pollen and weed pollen showed the highest in May (16.1%, 10.4%, respectively) and the lowest in March (7.0%, 4.9%, respectively). The monthly sensitization rate to house dust mite was the highest in September (49.7%) and the lowest in May (38.9%). The rates of sensitization to alternaria, cat and dog dander showed no seasonal differences.

Conclusion: The sensitization rate to 6 common aeroallergens showed a significant increase during the last 10 years in Korea, especially in case of tree pollen, weed pollen, cat and dog dander. These results might be attributable to climate and lifestyle changes.

TP1139 | The inner-city asthma in Zagreb: 2018 versus 2004

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Background: Children living in inner-cities are at high risk for developing asthma. Decreased biodiversity is considered to be the major etiological factor contributing to the disease development, although the underlying mechanisms are not well understood. The aim of the study was to explore the prevalence of asthma among children living in inner-city of Zagreb, Croatia, and to explore time trend prevalence form the last study (2004), using the same methodology.

Method: Original ISAAC questionnaires, consisting of questions on child′s demographic characteristics, core modules on wheezing and supplementary modules were completed by parents of 10 years 0 months-10 years 11 months children from 20 schools in the city of Zagreb in the school year 2017/2018. A total number of 343 questionnaires were returned and analysed.

Results: 343 children aged 10 years 0 months-10 years 11 months were analysed. 172 of them were boys and 171 were girls. Prevalence of reported diagnosis of asthma in our sample is 8%. In last 12 months, 6.1% patients had wheezing, while 7.9% of children used asthma medications (salbutamol and/or inhalant corticosteroids).

Conclusion: Comparing with the results from the study conducted in Zagreb in the same age group in 2002, our results showed statistically significant increasing in the prevalence of the diagnosis of asthma (χ2 6.7182, *P*-value 0.009544; $P < 0.05$), but no statistically significant increase in the prevalence of wheezing in the 12-months period (χ^2 0.0038, *P*-value 0.950619, $P < 0$ 0.05.).

TP1140 | Are new types of smoking alternatives better than conventional tobacco for the prevention of asthma in adolescence?

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Background: The health effect of electronic cigarette (e-cigarette) versus conventional tobacco is still under investigation. We evaluated the effect of smoking in the development of asthma according to many aspects of smoking including e-cigarette smoking.

Method: This study was conducted using the 14th Korea Youth Risk Behavior Web-based Survey (KYRBWS), 2018 which represented 2 850 118 Korean middle and high school students (12-18 years old). The development of asthma was assessed by the question "Were you diagnosed as asthma by physician within past 12 months?" Conventional and e-cigarette smoking status was assessed by corresponding questionnaires. Covariates were age, sex, body-mass index, physical activity, socioeconomic status, presence of rhinitis and secondhand smoking.

Results: There were 190 313 (6.7%) current smoker and 76 715 (2.7%) current e-cigarette users. Current smoking was significantly associated with the development of asthma (odds ratio [OR] = 1.53, 95% confidence interval [95% CI] 1.23-1.91) whereas current e-cigarette use was not (OR = 1.17, 95% CI, 0.83-1.63). However, when e-cigarette were divided into liquid and heating type e-cigarette, consumption of heating type e-cigarette was significantly associated with the development of asthma (OR = 1.55, 95% CI, 1.02-2.36). Using only e-cigarette and not conventional cigarette was not a risk factor for the development of asthma compared to never smokers. Switching to e-cigarette smoking from conventional smoking significantly reduced the risk of the development of asthma than maintaining conventional smoking (OR = 0.14, 95% CI, 0.2-0.96).

Conclusion: E-cigarette seemed less associated with the development of asthma than conventional smoking. However, the type of e-cigarette must be taken into consideration.

TP1141 | Progress in automated airborne pollen monitoring with the BAA500

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Background: In the last few years, an increasing percentage of the population suffers from pollen allergies. As yet, established pollen counting techniques rely on manual evaluations with light microscopes. Therefore, they cannot supply short-term information on ambient pollen concentrations which would be extremely helpful for allergic persons to plan their daily activities and medications. Since 2010, Hund has been active in the development and installation of the first fully automated pollen monitoring system, the BAA500. It is based on optical microscopy in combination with digital image acquisition and recognition.

Method: The implemented algorithm discriminates the pollen taxa contained in the machine database with high accuracy. As the images of the pollen are permanently stored in the system and because the evaluation of the taxa is based on a feature set, hitherto unknown species can easily be included into the database, and re-evaluation of images of older samples is always possible. The results are available on short-term basis and can easily be accessed via Internet.

Results: For many years now, the BAA500 has successfully been tested in several locations in Germany and Europe. Its results are continuously validated and improved. In 2018, the first pollen monitoring network has been established based on the BAA500. It has already been proven as a quantum leap for automated pollen monitoring. It will therefore be a key component for future pollen forecasting models. The BAA500 has shown high reliability and accuracy when compared with the result of Hirst-type traps. Thus, it helps affected persons with more precise pollen counts.

Conclusion: The presentation shows how the accuracy of the system can continuously be improved by adding more pollen data to the reference database. This is supported by pollen experts using our system. Moreover, the classification algorithm is open in the sense that also objects other than pollen can be detected and added to the database. We present first results for germs or fungal spores.

TP1142 | Automated dander dispersion in a naturalistic exposure chamber

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Background: A naturalistic exposure chamber with two neutered male cats has been developed (Red Maple Trials, Ottawa) to test allergic responses of subjects during controlled exposures to Fel d 1. To improve upon traditional methods of dander aerosolization,

in which bedding is shaken, resulting in transient levels of allergen, we have developed an automated delivery system using a modified robotic vacuum cleaner. The prototype model has been shown to deliver steady particle levels and Fel d 1 levels consistent with those found in homes with cats. In the present work, we validate our working aerosolization system for two dispersion rates, and document the spatial and temporal distribution of aerosolised particles and Fel d 1 within the chamber.

Method: The robotic vacuum has been modified to vent aspirated dander into the air via a custom fit exhaust tube. Controlled remotely, it will move throughout the chamber (floor area = 15.1 m^2) for up to one hour, aerosolizing the dander that has naturally collected on the floor. Air samples will be obtained at various locations across the chamber using portable air sampling pumps (Gillian 5000) with glass fiber filters (Millipore). Fel d 1 deposited on the filters will be quantified using ELISA (Indoor Biotechnologies). Counts and sizes of dander particles will be measured using a time-of-flight particle size distribution analyser (PSD 3603, TSI Incorporated). Results will be evaluated for spatial distribution and temporal stability of Fel d 1 level, for two dispersion rates.

Results: A flow visualisation test, in which the robot aspirated and vented flour dust, revealed a turbulent round jet exiting the vacuum, having a strong core as high as 2 feet above the floor, and high concentrations of diffused particulate as high as 4 feet above floor level. Preliminary testing of the working model at the highest flow setting showed a higher number of large particles (>1 μm) being aerosolized compared to a prototype model, with the average particle size approximately 2 μm, compared to 0.8 μm for the prototype model.

Conclusion: The validation of a novel automated system for aerosolizing dander is expected to provide a means of better controlling subject exposure to animal dander for cat allergy studies, while maintaining a naturalistic environment.

TP1143 | Comparison of Methods for cat dander aerosolization

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Background: Historically, aerosolization of cat dander in natural exposure rooms is done by intermittently shaking bedding. However, this has resulted in widely variable Fel d 1 exposure. For the RMT Natural Exposure Chamber, we developed an automated aerosolization technique, using a filterless robotic vacuum cleaner that generates more stable particle levels. In this study we compare cumulative airborne Fel d 1 levels and aerosolized particle counts from this automated method, with and without the use of additional fans, to the blanket-shaking method.

Method: Dander aerosolization was performed for 30 minutes for each method; the vacuum was run continuously, while bedding was shaken vigorously for two minutes at 15-minute intervals. During the 30 minutes of aerosolization (or two 15-minute periods following blanket shaking) dander samples were collected using portable air sampling pumps (Gilian 5000) at 4 L/min with 2 μm glass fiber filters (Millipore). Fel d 1 was quantified using ELISA (Indoor Biotechnologies). Counts and size distributions of airborne particles were measured every three minutes during and for 15 minutes following aerosolization with a time-of-flight particle size distribution analyser (PSD 3603, TSI Incorporated)). Measurements were repeated on four separate days for each method.

Results: Despite having the lowest total particle (>2 μm)count (3.04×10^6 particles/m^3,, blanket shaking resulted in the highest Fel d 1 levels of the three methods (76 ng/m^3). It also had the highest standard deviation (30 ng/m^3), indicating comparatively low repeatability. The vacuum method with fans produced comparable Fel d 1 levels (65 ng/m^3) as well as the lowest standard deviation (8 ng/m^3) with a particle count of 4.58×10^6 particles/m^3. Vacuuming alone had the highest particle count (8.06×10^6 particles/m^3), but also the lowest Fel d 1 levels (43 ng/m^3), showing that the Fel d 1 level did not correlate to aerosolised particle count.

Conclusion: All methods produced Fel d 1 levels in the range of those in homes with cats. Particle counts surprisingly did not correlate to Fel d 1 level, suggesting the aerosolization of non-dander particles. Blanket shaking generated the highest average Fel d 1 level, but showed low repeatability. The vacuum method with fans showed the best stability and repeatability and met target Fel d 1 levels for matching “in-home” conditions.

MONDAY, 3 JUNE 2019
TPS 30
URTICARIA AND ANGIOEDEMA II

TP1144 | Chronic spontaneous urticaria (CSU) associated with chronic inducible urticaria (CIndU): Efficacy of omalizumab

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Background: Omalizumab has been shown to be effective and safe therapy for antihistamine-resistant CSU isolated or associated with CIndus. We aim to assess the efficacy of omalizumab (300 mg/4 weeks) in patients with antihistamine-resistant CSU associated with one or more CIndUs.

Method: Retrospective analysis was conducted of outpatients treated at an urticaria reference center of a University Hospital. 11 patients with CSU associated with CIndUs who were treated with omalizumab 300 mg/4 weeks were enrolled. Response to omalizumab was assessed by UAS7 and negative physical stimulation provocation. It has also been assessed timing to response.

Results: All patients were female with age between 27-78 years old. Patients had following CIndUs: Symptomatic Dermographism (10), Delayed Pressure Urticaria (6), Cold Urticaria (1) and Heat Urticaria (1). Before omalizumab first dose, patients presented UAS7 11-42 (mean = 26.5). After first administration dose UAS7 was 0-4 (controlled urticaria) in 9 patients, who presented reduction or remission in 24-48 hours. Two patients didn't achieved urticaria control after first dose (UAS7 > 7) [uncontrolled urticaria], presenting UAS7 = 0 after second anti-IgE dose. All patients also evolved with negative physical provocation after omalizumab therapy.

Conclusion: Our data corroborates with running literature showing omalizumab use in refractory CSU associated with CIndUs patients is effective, allowing CSU and CIndUs control.

TP1145 | How to discontinue omalizumab in chronic spontaneous urticaria?

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Background: The clinical efficacy and safety of omalizumab in chronic spontaneous urticaria (CSU) has been demonstrated in several clinical trials and real-life studies. As of now, there is no consensus on when and how to discontinue omalizumab treatment in CSU patients who show complete response. Here, we assessed the response of CSU patients to treatment discontinuation by interval prolongation.

Method: We included 19 of 86 patients with CSU.

These 19 patients:

1). had been treated with omalizumab (300 mg/4 weeks) for at least 6 months
2). had controlled disease as defined by urticaria control test (UCT) scores of ≥ 12 and minimal intake of antihistamines (≤2 times/week).

In patients who continued to show controlled disease, we continued to increase the treatment intervals by one week per application.

If their CSU remained controlled after prolongation of treatment intervals to 8 or 9 weeks, we discontinued omalizumab treatment and monitored patients for relapse for 3 months.

In patients who showed uncontrolled disease after interval prolongation, we shortened the interval by one week per application until the disease was under control again.

Results: Of the 19 patients who tried, 9 successfully discontinued omalizumab treatment by interval prolongation, and did not show relapse of their CSU for at least 3 months after their last omalizumab.

	Interval prolongation and discontinuation were possible (n = 9)	Interval prolongation and discontinuation were not possible (n = 10)	*P*-value
Female gender; n (%)	8 (89)	8 (80)	1
Age; years (range)	40 (28-51)	33.5 (23-40)	0.24
CSU phenotypes; n (%)			
Wheals, no angioedema	5 (56)	6 (60)	1
Angioedema, no wheals	–	–	
Wheals and angioedema	4 (44)	4 (40)	
Duration of the disease before omalizumab; years (range)	7 (3-10)	3 (2-4)	0.034
Duration of the therapy (from first to last application); weeks (range)	33 (28-41)	47.5 (29-55)	0.1

Conclusion: In conclusion, in CSU patients with well-controlled disease and low AH intake, discontinuation of omalizumab treatment by prolonging the treatment interval may reduce relapse rates and limit the duration of relapse before re-initiation of treatment.

TP1146 | Low-responsiveness of basophils via FcεRI reflects disease activity and duration of disease in chronic spontaneous urticaria

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Background: The insufficient effect of H1-antihistamine in some chronic spontaneous urticaria (CSU) patients suggests that factors other than histamine are involved in the pathophysiology of CSU. Moreover, a central role for basophils in the pathophysiology of CSU has been hypothesized. However, few studies have focused on the relationship between basophil reactivity via FcεRI and disease activity in CSU patients. The primary objective was to assess basophil reactivity via FcεRI against anti-IgE and FcεRI stimulation in CSU patients, and its association with disease activity of CSU. The secondary objective was to investigate FcεRI expression and IgE binding on basophils from CSU patients.

Method: We analyzed 38 CSU patients, 29 patients with cholinergic urticaria, and 11 healthy controls (HCs). The surface CD203c expression with or without anti-IgE or FcεRI stimulation, and IgE and FcεRI (CRA1, CRA2)expression on blood basophils was evaluated. CSU patients were also classified into three groups by disease activity using the urticaria activity score (UAS) 7 (UAS7 0-6, mild; 7-15, moderate; 16-42, severe), and the above parameters were compared.

Results: The proportion of CD203c^{high} basophils following anti-IgE or FcεRI stimulation was lower in CSU patients compared with HCs and patients with cholinergic urticaria. It was lowest in CSU with severe group. Basophils from CSU patients had a higher FcεRI (CRA1) expression, although it was not closely related with the severity of CSU. Subgroup analysis revealed that CSU patients showing low-responsiveness of basophils via FcεRI exhibited a short duration of disease but severe disease activity.

Conclusion: Low-reactivity of basophils via FcεRI is characteristic in CSU patients. This attenuated reactivity is associated with severe clinical activity in CSU patients.

TP1147 | Basophil phenotypic and functional profiles of 31 patients with chronic spontaneous urticaria

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Background: Mast cell/basophil degranulation and IgE are at the center of the Chronic Spontaneous Urticaria (CSU) physiopathology most likely due to extrinsic triggering still to be elucidated in context of auto-immunity. The aim of this study was to characterize basophil phenotype and activation capacity in newly diagnosed CSU.

Method: 31 patients addressed for CSU, were compared to 29 age and sex matched healthy controls (HC). Peripheral blood basophils were phenotyped on flow-cytometry (CD203c, CD123, CCR3, CD163, CD46, CD59, CD244, CD252) and Basophil Activation test using CD203c/CD63 labelling (Basotest, ExBio, Czeck rep) analysed on Navios (Beckman Coulter Fullerton CA).

Results: Fourteen (45%) patients had dermographism and 4 (13%) mechanical triggering. Twenty (65%) were female; mean age was 48.4 + 17.5 (19 to 85) years; 4 patients (16.7%) and 3 HC (10.3%) had past allergy. CSU was present for 4.8 ± 5.4 (0 -21) years and were all graded moderate to severe according to Urticaria Activity Severity (UAS7 = 25.8 + 10.0) and uncontrolled according to Urticaria Control Test (UCT = 3.7 ± 2.9). The mean Body Mass Index significantly higher (27.0 + 4.7 kg/m²) than in HC (24.3 + 4.51, $P = 0.030$) but not correlated to UCT or UAS7.

Serum IgE were raised in 42% CSU and 12% HC ($P = 0.0224$). Serum Tryptase mean levels were note elevated (5.8 + 4.2 µg/L) similar to HC (4.7 + 1.8 µg/L). D-dimers were increased in two groups (1057 ± 2018 u vs 589 ± 1092 u, NS). Basophils were rare in 32% CSU and in 7% of HC ($P = 0.0141$). Half maximum induced Baso degranulation (CD63 +) was obtained on 4.4 + 4.2% compared to 27.1 + 19.1% of basophils, $P = 0.0001$. Baso phenotypes were homogeneous for each marker tested. Complement regulatory molecule MCP (CD46) was downregulated in CSU with higher tryptase (still within normal ranges) and DDimers. OX40L expression was significantly reduced on CSU basophils and on several other lineages also, in association with lower expression of CD123c, CCD3, CD203c, 2B4 regulatory protein (CD244) and complement regulatory proteins. OX40L deregulation could reveal a cell mediated immunoregulation and a less severe UCT.

Conclusion: The biological analysis or peripheral basophils brings arguments for CSU heterogeneity with diverse possible mechanisms involving immunoglobulin (with modulation of IgG receptors, complement regulatory proteins, scavengers) but probably alternative cell mechanisms involving OX40L, 4-1BBL, regulatory receptors, explaining differences in anti IgE biotherapy efficacy.

TP1149 | Our data on the link between chronic urticaria and helicobacter pylori

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Background: Chronic urticaria (CU) manifests with urticarial rash for 6 weeks and longer. Several factors consider causative for CU but the causes of the most cases stay unknown. According to recent data *Helicobacter pylori (H. pylori)* infection also plays a role in pathogenesis of CU. The aim of our study is to define the prevalence of *H. pylori* infection among patients with CU and to investigate how does the eradication of *H. pylori* impact on the treatment of CU.

Method: The diagnosis of CU was verified in accordance with clinical criteria. All standard and specific diagnostic tests were carried out including the assessment of *H. pylori* by serological tests and gastroscopy. The triple schemes of eradication were performed for 10 days to the patients with revealed *H. pylori* infection in the frame of the CU treatment. The success of eradication was assessed by a decrease in antibody titers 3 months after the treatment. The patients were clinically assessed in accordance with current CU guidelines. Study was performed between January 2017 and June 2018 by informed consents of all patients.

Results: Sixty-one patients (45 females and 16 males, mean age 34.9 years) with CU were studied. Nineteen (31.2%, n = 61) of patients were diagnosed by inducible urticaria with different (mainly physical) inductors and 42 (68.8%, n = 61) - with idiopathic urticaria as the exact causes were not revealed. Twenty-two (36.1%, n = 61) of the CU patients were positive for *H. pylori* with the following distribution by groups: 6 (31.6%, n = 19) - inducible urticaria and 16 (38.1%, n = 42) - idiopathic urticaria. The eradication was successful in 19 (86.4%, n = 22) of the patients. The clinical assessment of successfully eradicated CU patients showed improvement in 15 of them (79%, n = 19): 2 (33.3%, n = 6) of inducible and 11 (68.8%, n = 16) of idiopathic urticaria patients. The remission was complete only in 4 patients (21.1%, n = 19) with idiopathic urticaria.

Conclusion: Despite contradictory data of previous studies our investigation revealed an association between CU and *H.pylori* and influence of eradication on the treatment of CU. The results are unclear in relation to different types of CU because of small number of patients. Nevertheless the prevalence of *H. pylori* is higher and the eradication seems more effective in patients with idiopathic urticaria. Thus, we can conclude that the definition of *H.pylori* and eradication need to be recommended in diagnostic and treatment schemes of chronic especially idiopathic urticaria.

TP1150 | Worsening of chronic spontaneous urticaria after intake of hot pepper

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Background: Patients with chronic spontaneous urticaria (CSU) have been reported to experience increased disease activity in response to the oral intake of hot pepper. As of now, it is unclear how common this is. Therefore, we assessed patients with CSU for the prevalence of disease worsening after the intake of hot pepper and characterized its effects on their urticaria.

	Overall	With worsening of urticaria after intake of hot pepper	Without worsening of urticaria after intake of hot pepper	P
Patients; n	85	39	46	
Age; years ± SD	39.1 ± 11.9	40 ± 13.2	38.4 ± 10.7	0.69
Female gender (%)	62 (73)	31 (80)	31 (67)	0.23
Co-existing diseases (%)				
Atopic	4 (5)	3 (8)	1 (2)	0.34
Autoimmune	6 (7)	4 (10)	2 (4)	
Duration of urticaria; years ± SD	3.9 ± 4.4	3.7 ± 4.4	4 ± 4.4	0.5
Treatment for CSU (%)	73 (89)	31 (84)	42 (93)	0.17
St-sgAH	31 (38)	17 (46)	14 (31)	0.18
Hi-sgAH	18 (22)	9 (24)	9 (20)	0.79
Omalizumab	24 (29)	5 (14)	19 (42)	0.007
Disease control status at the time of study (%)				
Controlled	55 (67)	24 (65)	31 (69)	0.81
Uncontrolled	27 (33)	13 (35)	14 (31)	

Method: A questionnaire-based survey study in adult patients with CSU and a history of hot pepper consumption was carried out at a reference center for urticaria in Turkey. CSU patients who had co-existing chronic inducible urticaria were excluded from the study.
Results: Of the eighty-five patients with CSU included in this study, 46% (39 of 85) reported worsening of their urticaria after consuming hot pepper. Demographic features, duration of CSU and control status of urticaria were not different between patients who experienced worsening of their urticaria after the intake of hot pepper and those who did not. In affected patients, worsening of their symptoms started 1.2 ± 1.2 hours after the intake of hot pepper and lasted for 3.3 ± 6.8 hours. Symptoms disappeared significantly faster in patients who took antihistamines after worsening of their urticaria with hot pepper (0.7 ± 0.6 vs 5.8 ± 8.8 hours; $P = 0.003$).
Conclusion: Worsening of urticaria is common and relevant in patients with CSU in Turkey. Further studies are needed to explore if this is also the case in other geographical regions and to identify and characterize the underlying mechanisms.

TP1151 | CSU treatment with omalizumab in a pediatric patient

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Case report: Omalizumab is effective and well-tolerates for chronic spontaneous urticaria (CSU) treatment and it has been approved and recommended for anti-histamine (AH) refractory CSU in over 80 countries for adults and children > 12 years-old. It has also been approved for asthma treatment in children 6-12 yo. Safety in patients younger than 6 yo is not established. We report a case of AH refractory CSU in a 4 yo successfully treated with omalizumab.
3 yo girl referred to Allergy and Immunology center due to itchy wheals, which started 6 months before first appointment. They resolved temporarily with 1st generation AH. Laboratory results: 575 eosinophils/mm^3; normal thyroid hormones and negative antithyroid antibodies; ESR 5 mm; negative antinuclear factor and rheumatoid factor; negative serology for hepatitis; total serum IgE 338 kUI/mL; D-dimer 896 n/mL. She also had positive autologous serum skin test (5 × 4 mm). She was prescribed continuous 2nd generation AH for 4 weeks, with no improvement The mother reported increased appetite as a side effect. AH dosing was doubled, and she returned 4 weeks later, unresponsive and requiring weekly doses of oral steroids. Different AH were prescribed, along with montelukast, but she remained symptomatic and with high UAS 7 scores. Cyclosporin A was also tried for 2 months, with no response. When she was 4 y9 m old, omalizumab 150 mg/month was initiated and in the same day of the first application, the lesions resolved entirely and remained so until now (8 months later) and no side effects were observed.
Conclusion: omalizumab has not been approved for CSU treatment in children, but may be a good option for severe cases. More controlled studies are needed to establish safety.

TP1152 | Cold Urticaria In Children

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Background: There are no data on the features of cold urticaria in children depending on different sensitivity to cold. The aim of the study: to evaluate clinical features of cold urticaria in children with different temperature sensitivity (TS) to cold.
Method: diagnosis of cold urticaria was established using the Temp Test® 3.0 Prototyp, Emosystems, GmbH apparatus. All the patients were divided into two groups: group 1 included children with low TS - from + 4 to + 12°C (n = 16), group 2 included children with high TS - from + 14 to + 28°C (n = 9). Statistic analysis was performed with Mann-Whitney criteria, 95% of credible interval.
Results: In children with low TS, the average Temp Test was 8.31 ± 1.34°C and in children with high TS it was 17.1 ± 2.55°C ($P \leq 0.01$).
Average age of children with low TS was 8.4 ± 1.99 years, average age of children with high TS was 12 ± 2.10 years ($P \geq 0.05$). Average duration of disease in group 1 was for 1.4 ± 0.97 years, in group 2 it was 1.23 ± 1.35 years ($P \geq 0.05$). Cold urticaria in children of group 1 began at the age of 7.1 ± 0.94 years and in children of group 2 it began at the age of 10.7 ± 2.21 ($P \geq 0.05$) years. Clinical manifestations of cold urticaria as localized condition are found in group 1 in 68.7 ± 23.47% of children and in 55.5 ± 34.4% of children in group 2 ($P \geq 0.05$). Systemic manifestations were noted in 31.3 ± 23.5% of children in group 1 and in 44.4 ± 34.4% of patients in group 2 ($P \geq 0.05$). There is a tendency both of increase in systemic manifestations of cold urticaria and its combination with angioedema in children with high TS. Combination with angioedema is observed in 18.7 ± 19.7% of children in group 1 and in 55.5 ± 34.4% of children in group 2. Other types of chronic urticaria (chronic spontaneous, symptomatic dermographism) were revealed in 37.5 ± 24.5% of children in group 1. As for children of group 2 urticaria combinations occurred in 22.2 ± 28.8% of them.
Case history of patients proved that atopic diseases (allergic rhinitis, bronchial asthma, atopic dermatitis) occur in 50 ± 25.3% of children with low TS. As for children with high TS they occur in 66.7 ± 32.6%.
Conclusion: Regardless of the degree of temperature sensitivity cold urticaria in children occurs at the age of 7.1 ± 0.94 -10.7 ± 2.21 years on average and lasts less than 2 years. Clinically cold urticaria in half of children occurs in a localized form. At the same time in children with high temperature sensitivity tendency to combination of urticaria with angioedema was revealed.

TP1153 | Cold urticaria in a child with familial mediterranean fever

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Case Report:

Background: Familial Mediterranean fever (FMF) is an autoinflammatory disease characterized by recurrent attacks of fever and poly-serositis. Skin manifestations are rare during FMF attacks. The only cutaneous manifestation of FMF is erysipelas-like erythema which mostly occurs around the ankles. Cutaneous rash during attacks suggest diagnosis of other autoinflammatory diseases such as cryopyrin-associated periodic syndrome (CAPS). Urticarial rash is commonly observed in CAPS attacks triggered by cold in a subclass of CAPS called familial cold associated syndrome (FCAS). Cold-induced urticaria is a chronic physical urticarial triggered by cold. Ice cube test is positive in cold-induced urticaria while it is negative in FCAS.

Case report: A 12-year-old boy admitted to our hospital with recurrent attacks of fever, abdominal pain, chest pain, and urticarial rash. He was having these attacks since he was 3 years old. He had been using colchicine since he was 4 with the diagnosis of FMF and the attack frequency significantly decreased with colchicine treatment. He was having only 1-2 attacks per year after colchicine initiation. He was compound heterozygous for M694V and R761H mutation on *MEFV* gene. With the clinical findings and the results of the genetic analysis, the FMF diagnosis was certain; however, it was atypical that he had urticarial rash during attacks. His mother explained that he had the urticarial rash only in the locations where she applied cold cloths when he had fever. He also had this rash between the disease attacks when he contacted something cold. With these details mentioned, we suspected cold urticaria and performed ice cube test which was positive. We made the diagnosis as the co-occurrence of cold-induced urticaria with FMF. The family was informed about the necessity of not being cold contact.

Conclusion: Our patient was experiencing high fever attacks typical for FMF and his mother was applying cold cloths which triggered the cold-induced urticaria. In FCAS, the attacks are triggered by general cold exposure such as air-conditioned rooms or cool breezes; not by localized cold exposure. It is very important to get the details of symptoms described by the patient/parents as a part of typical attacks in monogenic autoinflammatory diseases to make the differential diagnosis. Some symptoms such as urticarial rash in our case may appear as a result of a concomitant disease rather that the underlying disorder.

TP1154 | Clinical experience of a chronic urticaria referral university center

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Background: There are few studies on chronic urticaria (CU) in Brazilian population. Information of clinical profiles and therapeutic management can be of great value for researchers and the daily practice of general practitioners or specialists. The aim of this study was to describe the routine procedures, clinical profile and evolution of CU patients treated in a reference center.

Method: A retrospective analysis of standardized clinical records of CU patients registered between March 2011 and February 2016. The variables evaluated were: gender, age, comorbidities, type and duration of urticaria, Urticaria Activity Score (UAS), Chronic Urticaria Quality of Life Questionnaire (CU-QoL), results of provocation tests and autologous serum/plasma skin tests (ASST/APST) and treatment at the first visit. Patients with 3 or more visits were selected to analyse disease evolution, used drugs, UAS and CU-QoL scores also in the last visit.

Results: Study population comprised 200 CU patients with median age 45 years (perc25-75 = 27-58 years, range: 5-82 years) and 162 (81%) female. The median duration of symptoms before diagnosis was 24 months (perc25-75 = 9-60 months). One hundred and sixty-six patients (83%) had chronic spontaneous urticaria (CSU) and 100 (50%) had chronic inducible urticaria (CIndU). CSU was associated with CindU in 66 (33%) patients. ASST and APST were performed in 76 and 73 patients with 41 (53.9%) and 28 (38.3%) positive tests, respectively. Angioedema was described in 112 (56%) patients. The first prescription to 179 (89.5%) patients was monotherapy with antihistamines and associations with other medications were prescribed to 21 (10.5%) of them. Among the 123 followed-up in three or more visits, 94 (76.5%) received antihistamines, and 29 of these (23.5%) used associations. In this followed up group the average results of initial and final UAS and CU-QoL scores were 1.38 ± 1.76 and 0.73 ± 1.4 (0-6), and 34.27 ± 21.53 and 21.76 ± 19 23 (0-100), respectively.

Conclusion: The majority of patients had the diagnosis of CSU, frequently associated with CIndU. All patients were treated with antihistamines and there was a great need for updosing and also for combination with other medications. We observed satisfactory improvements in UAS and CU-QoL scores.

TP1155 | Differential diagnostics of chronic urticaria and urticarial vasculitis by hyperspectral imaging

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Background: Any properly diagnosed disease with its causes is a principal factor that has a direct effect on efficiency of treatment procedures and on their economic component. Not rarely are the situations where etiologically different diseases show a symptom-similar clinical pattern. An example of such developments is the situation with *chronic spontaneous urticaria* (CSU) and *urticarial vasculitis* (UV). According to various researchers, 2% to 25% of patients who were examined for SCU are suffering UV. The difficulties of the CSU and UV differential diagnostics are caused by similar clinical symptoms, subjective histological examination and strong dependence on the skills of a medical practitioner who conducts such examination; and by differences in diagnostic approaches to medical treatment of CSU and UV. This problem has become especially essential in connection with the biological therapy introduced into clinical practices. The histological examination of skin biopsy slices is currently a "golden standard" in the UV diagnostics. However, the deficient outcome of information obtained by routine histological techniques can, on some occurrences, result in wrong diagnoses. It means that the said techniques need to be further developed and improved.

Method: For the purposes of solving the said difficulty, it is proposed to introduce the hyperspectral imaging and analysis of histological specimen into the histological practice. The paper has evidenced that rising the information response and reliability of standard methods is achievable by using in the optical scheme a microscope of separable hyperspectral module based on a tunable acousto-optical filter. The work has resulted in taking spectral images of a H&E stained cross-section of human skin and in rated spectral transmission responses of different skin layers.

Results: The report presents examples of recorded test images, histological sections and calculations of spectral responses for different skin layers and for a number of diseases.

Conclusion: The designed hyperspectral module enhances significantly the functional capabilities of modern laboratory microscopes and rises the reliability level of the chronic urticaria and urticarial vasculitis differential diagnostics.

TP1156 | Clinical profile of patients with spontaneous chronic urticaria in a federal university hospital in Brazil

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Background: Chronic urticaria is defined as that urticaria that persists for more than 6 weeks and is a very frustrating condition for both patients and their families. Despite the impact on quality of life and the morbidity associated with chronic urticaria, much remains to be known about this disease.

Method: A descriptive study was conducted in Antonio Pedro University Hospital, Brazil. It included patients diagnosis as spontaneous chronic urticaria on regular follow-up during the study period (January 2018 to December 2018). These were investigated regarding their demographic details and clinical feature

Results: Forty-three patients with spontaneous chronic urticaria were included, their mean age was 44.33 (14-79). Females made 74.41% of patients. The median time living with urticaria until the first visit in our hospital was 19 months (interquartile range 8-66). The presence of comorbidities was found in 69.7% of the patients. The most frequent comorbidity was systemic arterial hypertension. The presence of autoimmune disease was observed in only 11.6% of the patients. Coexisting angioedema and inducible urticaria was observed in 16.3% and 55.81% of the patients, respectively.

Conclusion: There is a need to raise awareness about spontaneous chronic urticaria. We found in our study a late referral of the cases to a specialized center. The disease represents a personal burden but also has a social impact since it affects periods of life where is more social engagement and productivity.

TP1157 | Omalizumab treatment of recalcitrant delayed pressure urticaria

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Case Report:

Introduction: Delayed pressure urticaria (DPU) is defined by the appearance of skin swelling after the application of sustained pressure to the skin and belongs to a group of chronic inducible urticarias (CindU) - chronic urticarias, in which hives and angioedema occur after exposure to a specific trigger. CPU is usually nonpruritic, characterised by pressure-induced pain and burning, that occurs 4-6 hours after exposure and causes significant impairment in quality of life. Omalizumab is a monoclonal anti-IgE antibody, currently approved for the treatment of chronic spontaneous urticaria

in patients, resistant to H1 antihistamines. We present a patient with isolated DPU, successfully treated with off-label omalizumab.

Materials and Methods: 40-year old otherwise healthy male presented to our clinic with a one year history of painful swelling and erythema on sites of pressure. Severe symptoms of DPU (swelling of the hands, feet and buttocks) prevented daily activities. He had no known allergies. For approximately one year he had been treated with four times the standard recommended dosage of loratadine and then cetirizine with insufficient response.

Results: Blood tests (complete blood cell count with differential, thyroid function tests, Borrelia burgdorferi serology, rheumatoid factor) as well as abdominal ultrasound did not reveal any abnormalities. Inducible urticaria tests, performed in 2016, were negative for symptomatic dermographism, cold, heat and cholinergic urticaria. DPU test performed with dermographometer at 100 g/mm^2 was positive (erythema and oedema) when applied for 30-60 s. The patient has been treated off-label with omalizumab 300 mg every 4 weeks since June 2017. We observed 50% reduction of symptoms after the first dosage. The patient is currently symptom free in between applications. DLQI dropped from 28 points (June 2017 -before treatment with omalizumab) to 0 (last visit January 2019).

Repeated testing with dermographometer at 100 g/mm^2 8 days after last omalizumab dose was negative. We observed mild erythema and no oedema at 60 s and 70 s, while shorter times (10-50 s) showed no reaction at all.

Conclusions: The excellent response to omalizumab observed in this case supports its efficacy and tolerability for the treatment of refractory DPU. Written informed consent for publication of these clinical details and/or clinical images included in my abstract presentation was obtained from the patient.

TP1158 | Management of histaminergic disorders: The contribution of the immunoallergist illustrated through 5 cases

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Background: Chronic urticaria (CU) and histaminergic angioedema (HA) are frequent and sometimes indicative of immunoallergic diseases.

Method: We present a series of 5 cases with CU and/or HA, either resistant to a first-line treatment with antihistamine or associated with extracutaneous symptoms.

Results: The first patient was diagnosed with a monoclonal mast cell activation syndrome, due to extracutaneous symptoms of chronic mast cell activation, eosinophilia, high serum tryptase level and *KIT* D816V mutation with no B or C findings.

The second case was a chronic spontaneous urticaria (CSU) worsened by a Hashimoto's thyroiditis with monoclonal gammopathy of undetermined significance (MGUS), discovered during the additional investigations performed because of antihistamine resistance and cold triggering.

The third patient was diagnosed with a hypocomplementemic vasculitis (MacDuffie), due to the association of asthenia, inflammatory polyarthralgia with arthritis, hypocomplementemia with low serum C1q level and persistent anti-C1q auto-antibody.

The fourth case leaded to diagnose a hypersensitivity to α-gal, because of atypical chronology (evening hives attacks and recurrent urticaria during the first weeks), systemic symptoms (anaphylactic reactions, serum sickness-*like* reaction after tick bite) and positive allergy assessment (skin prick tests to mammalian kidneys and meats, cetuximab intradermal test, and specific IgE to α-gal).

The fifth report was a patient with a CSU resistant to third-line treatment (with Omalizumab), with systemic symptoms (Raynaud phenomenon, arthralgia, dry eye syndrome, purpura in the past), C-reactive protein at 24 mg/L and a positive serology to *Toxocara* (with an ineffective antiparasitic treatment). Because no other disease was found, including autoimmune disorders and vasculitides, cyclosporin A was given to the patient with efficacy.

Conclusion: Although few investigations are recommended in histaminergic disorders, additional investigations looking for immunoallergic disease appear useful in various situations, such as a resistance to treatment, extracutaneous or systemic symptoms, an atypical chronology or some specific triggers (cold, physical effort). The immunoallergist has an essential role to play as a second-line actor in the diagnostic and therapeutic management of the patients with CU and/or HA.

TP1159 | Cases of contact dermatitis mimicking angioedema

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Case Report:

Background: Angioedema is a vascular reaction involving the lower dermis, subcutis and/or submucosal tissue and causing a temporary localized swelling in any part of the body. For many health care professionals, the diagnosis presents an ongoing challenge; several diseases like contact dermatitis may manifest with subcutaneous or submucosal swelling and falsely be assumed to be angioedema. The clinicians at the emergency department and in the immunology/allergy clinics must be skilled at recognizing the features of

angioedema and its differential diagnosis. Here we reported 2 patients diagnosed contact dermatitis with their history and physical examination.

Case series: Two adolescent girls were referred to our clinic from pediatric emergency department with the diagnosis of angioedema. Physical examination revealed marked edema and erythema, especially in the periorbital region and eczematous lesions on the scalp. Patient 1 was dyed her hair two days ago and 2 hours later serous discharge started at the scalp. After 24 hours, edema was developed firstly her forehead then developed all over the face. It was learned that she had previously dyed her hair 2 more times. Nine months ago, in her first hair dying no reaction was observed. Five months ago, in her second hair dying there was a serious discharge in her scalp for 2 days and then she was cured. Patient 2 was dyed her hair five days ago and had complaints of swelling, redness and burning around the eyes. It was learned that she had previously dyed her hair 2 more times. She had erythema of the scalp in her first hair dying and had eczematous lesions on the scalp in her second hair dying. Contact dermatitis was considered secondary to hair dye in the light of the history and clinical findings. They were started on methylprednisolone and antihistaminic treatment. Edema disappeared within 3 days. Patients were informed about need to stay away hair dye.

Discussion: Contact dermatitis due to hair dye is often confused with angioedema because of its edema in the face and especially in the periorbital region. Contact dermatitis should be considered in the differential diagnosis of patients presenting to the emergency department with edema, especially in the periorbital area, and the history of hair dying should be investigated.

TP1160 | Urticaria-angioedema paraneoplastic syndrome associated with renal cells carcinoma

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Case report: We present the clinical case of a 46 year old woman reporting *de novo* spontaneous generalized urticaria and facial angioedema arising several months after initiation of progressive fatigue and adynamia of unknown cause, in the absence of any other warning signs, namely weight loss or anorexia. Angioedema was predominant on eyelids, lips and tongue, usually waned since early morning until afternoon and occurred about three times a week for 3 months with a severity that varied from minor to severe. There was no clear association with any specific food, drug, insect sting, physical activity or other known urticaria inducer. Apart from urticaria and angioedema manifestations, clinical examination showed no major abnormality. Anti-histamines were effective on urticaria control but had no effect on improving facial angioedema. Spirometry and thorax x-ray were both normal. Blood tests revealed normal red and white blood cell counts as well as normal renal, liver and thyroid function. Sedimentation rate, complement serum proteins (C1, C4 and C1q) and C1-esterase inhibitor concentrations were within normal ranges. A thoraco-abdomino-pelvic CT-scan revealed a 4.8 cm diameter cyst at a supero-posterior position in the right kidney, deemed as a probable renal cells carcinoma at a subsequently performed Uro-CT scan. A radical nefro-ureterectomy was successfully performed and tumor histology established a chromophobe renal cells carcinoma diagnosis at a pTNM pT1b Nx R0 staging according to the American Joint Committee on Cancer (8° edition). A few days after surgery, a fast improvement of facial angioedema was observed and one month later its complete disappearance was ascertained, without any recurrence during a subsequent one-year follow-up.

Comments: Chronic spontaneous urticaria could arise in association with systemic or organ-confined neoplastic diseases, configuring a possible paraneoplastic syndrome. Around 25% of renal cells carcinoma patients will develop a paraneoplastic syndrome but quite rarely urticaria and/or angioedema. This clinical case highlights the relevance of a correct diagnostic workup in chronic spontaneous urticaria patients, particularly when atypical characteristics are prominent and accompanied by unspecific systemic disease warning signs.

TP1161 | A very unexpected cause of chronic urticaria

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Case report: Hypersensitivity reactions (HSR) to folic acid are rare and chronic urticaria induced by folic acid rich foods is even more rarely reported.

A 36 year-old female patient was referred to our department due to exacerbation of chronic urticaria after ingestion of strawberries. As comorbidities, we highlight a radicular syndrome, with the need of chronic pain medication (gabapentin and cyclobenzaprine), and a severe lung emphysema due to tobacco. Since 2016 she had frequent episodes of urticaria with no evident trigger, denying worsening with anti-inflammatory drugs. In addition to the exacerbation of urticaria following the ingestion of strawberries, she also reported one reaction to folate supplement with dyspnea, facial edema and generalized pruritus and erythema 15-30 minutes after taking one 5 mg tablet. She recurred to the emergency department, where only a generalized pruriginous exanthema was described, with no other findings in physical examination. She received treatment with antihistamines and corticosteroids with symptom resolution and she never took folate supplements again. We assumed the diagnosis of chronic spontaneous urticaria and, in order to investigate the hypothesis of concomitant drug allergy, we performed an oral drug

challenge with folic acid. Thirty minutes after ingestion of the first dose (1 mg), the patient developed generalized urticaria, with no other manifestations - 10 mg cetirizine and 40 mg prednisolone were administrated with resolution of the symptoms within three hours. Skin prick test and specific IgE to strawberry was negative. She was given indication to avoid folic acid supplements and supplemented food or drinks and, since then (7 months follow-up), she had only one more episode of urticaria, related to the ingestion of broccoli and beans, which are folate rich foods, such as strawberries.

The presentation of this case is relevant because folic acid HSR are very rarely described as a cause of chronic urticaria. These findings should raise awareness for possible immediate allergic symptoms caused by folic acid-containing foods in patients with folic acid allergy. Written consent to share clinical information was given by the patient.

TP1162 | Allergy profile in patients with urticaria in Reunion Island

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Background: Urticaria is a complex problem and the most frequent skin disease. Although urticaria can result from several causes, a possible relationship between urticaria and atopy has been suggested.

Method: 85 patients with urticaria (males 35) in the age range of 22-55 years were evaluated for evidence of atopy. 82% of the patients has urticaria for 3 months or more. 42% of the subjects had daily symptoms. Skin Prick Test (SPT) was performed in our Allergy outpatient clinic. All patients underwent SPT to predefined panel aeroallergens: house dust mite- D.Pteronyssius, D.Farinae and Blomia Tropicalis (HDM), cat, moulds, grass and tree pollen allergens with saline and Histamine controls.

Results: Coexistent allergic conditions included Allergic rhinitis (42%); Asthma (18%); Drug allergy (4%); contact dermatitis (12%). Family history among the first degree relatives was positive in 24% for atopy and 9% for urticaria. 52% of the subjects (44/85) had positive SPT to HDM. Out of 40 patients with urticaria and no co existent allergies 21 (52%) subjects reacted positively to HDM antigens. Out of 45 patients with urticaria and coexistent allergies 41 (91%) reacted positively to HDM antigens.

Conclusion: Sensitization to HDM is frequent in patients with urticaria. Atopy needs to considered in the evaluation of patients with urticaria in tropical countries.

TP1163 | Urticaria and urticarial vasculitis: 2 entities, the same trigger

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Case Report:

Summary: Urticaria is a common disease, characterized by maculopapular lesions and/or angioedema. It can be triggered by physical factors like cold. The urticarial vasculitis is a clinicopathological disease characterized by clinical manifestations of urticaria accompanied by clinical manifestations of Leukocytoclastic vasculitis.

Case report: A 28-years-old white woman with history of Systemic Lupus Erythematous (SLE) diagnosed in 2010 medicated with Prednisolone 5 mg/d and Hydroxychloroquine (400 mg/d) was presented with recurrent episodes of cold's cutaneous reaction. The reaction consists in maculopapular pruritic lesions in areas exposed to cold air, liquids and surfaces; angioedema of lips with ice cream ingestion; punctual purpuric lesions that converges in bigger plaques with edema and sensation of burn located in legs when contacted with cold. Of the carried out study: negative serologies and viral markers, normocomplement (C3 99.9 mg/dL, C4 411.1 mg/dL, C1q 14.8 mg/dL), IgE 587IKU/L, negative cryoglobulins and crioaglutinins and normal capillaroscopy. Cold provocation Tests, namely the Ice Cub test, showed a maculopapular lesion of 35 × 35 mm after 2 minutes of stimulation, and Temp Test® showed reaction to temperature below 18°C. A skin biopsy of a lesion revealed superficial and deep perivascular and interstitial polymorphonuclear infiltrate with leukocytoclasis, nuclear dust, and red blood cell extravasation. It was initiated measures to avoid skin exposure to cold and preventive treatment with 2nd generation anti-histaminic H1 without clinical improvement and with maintenance of the results of cold provocation tests.

Discussion: Unlike most of the cold urticarial patients, this patient did not show a good answer to preventive treatment which can be explained by the cold urticaria and urticarial vasculitis being secondary of SLE.

Conclusion: With this case, we want to demonstrate that the same trigger, the cold, can trigger different diseases in the same patient: the cold urticaria and the Urticarial vasculitis in a young woman with SLE.

MONDAY, 3 JUNE 2019
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AIRBORNE ALLERGENS

TP1164 | Grass pollen potency in ambient aerosol; grass pollen counts; seasonal allergic rhinitis; meteorological factors and pollutants in Madrid, Spain, during 2009 and 2010

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Background: Increasing temperatures lead to earlier and longer pollen and allergy seasons, due to more frost-free days and earlier and longer flowering seasons. Higher temperatures also increase ozone (O_3) production, which sensitizes the respiratory tract to allergens. More fall-winter precipitation further contributes to increased pollen production. The aim of this study was to compare the specific quantification of Phl p 1 and Phl p 5 aeroallergens and their potency, to *Poaceae* pollen counts and their potency, so as to establish their association with meteorological factors, pollutants and symptoms in patients with seasonal allergic rhinitis.

Method: The Hirst method sampler and the Burkard Cyclone sampler were used for pollen count and allergen quantification, respectively. The aerosol was extracted and quantified for Phl p 1 and Phl p 5 content using enzyme-linked immunosorbent assay procedures (the potency was defined as allergen per daily grass pollen count). The sampling period ran from 23rd March 2009 to 27th July 2010. An electronic card was used on a daily basis by 23 patients with relevant clinical sensitization to grass pollens during the last two years (score: 0- absence of symptoms; 1- mild symptoms; 2- moderate symptoms; and ≥ 3 -severe symptoms). Descriptive statistics of the same variables in 2009 and 2010, study periods, and non-parametric paired samples (Wilcoxon test - SPSS24 package) were used as variables that did not fit normal distribution, to allow any significant differences to be seen at the two observation points for each variable studied. A categorical principal component analysis model (CatPCA - SPSS24 package) was also carried out.

Results: The presence of atmospheric Phl p 1 and Phl p 5, is mainly confined to the period when grass pollen grains are present. The mean symptom score value in 2009 was 1.34 and in 2010, 0.92. Despite higher pollen grain counts in 2010, the higher symptom score in 2009 could be explained by the higher allergen potency observed in 2009 vs 2010 in Phl p 1 (70.03 pg/pollen vs 47.80 pg/pollen, $P = 0.025$). The CatPCA analysis explains around 45.39% of the variance. During the period studied, the strongest relationships were between symptoms and grass pollen counts ($R = 0.508$), and temperature and O_3 ($R = 0.522$).

Conclusion: The higher pollen potency in 2009, together with the effects of temperature and pollution (mainly O_3), could contribute to the higher seasonal allergic rhinitis symptom score observed in 2009.

TP1165 | Patterns of google trend terms related to reporting rhinitis and the ragweed pollen season in Ukraine

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Background: Google Trends (GT) may represent a new approach to assessing pollen allergy. However, the development of a pan-European sentinel network has raised a problem of translating terms into different languages. A precise definition of the pollen season onset is crucial for the confirmation of a pollen allergy diagnosis and personalized treatment. Ragweed pollen allergy was investigated due to its high allergenicity and widespread expansion in Europe. This study aimed to examine translations of "ragweed" and "hay fever" into native Cyrillic languages, especially Ukrainian and Russian, and to compare the seasonality of queries in Ukraine with ragweed and mugwort pollen counts.

Method: GT was used to search Google queries concerning ragweed allergy: "allergy", "hay fever", "running nose", "ragweed" "asthma" and "pollen". The Cyrillic terms in Ukrainian and Russian were used. Pollen collection for 2013-2015 was conducted using volumetric methods. Average daily temperatures were obtained from the web-site http://gismeteo.ua. Correlations were studied by using Pearson and Spearman tests.

Results: GT queries profile had the "B" pattern according to the classification developed by Bousquet J. et al (2017). A peak of "ragweed" queries was observed after the maximum of average daily temperature. The terms "allergy", "hay fever" and "ragweed" in Cyrilic are required in Ukraine to calculate the ragweed pollen exposure by GT. The ragweed pollen season started with a concentration of pollen grains of 12.95 m^{-3}. The *Artemisia* pollen season started between 19-25 days before the beginning of the *Ambrosia* pollen season.

Conclusion: GT may be a useful tool in the differentiation of the pollen seasons, especially when they overlap as in the case of *Artemisia* / *Ambrosia*. Three terms- "allergy", "hay fever", and "ragweed"- (in Cyrillic equivalents) are required in Ukraine to account for ragweed pollen exposure. The combination of GT tools with pollen counts may be used in large-scale epidemiological studies.

TP1166 | Olea pollen count in a changing climate, 38 years of observation

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Background: Global warming is currently related to climate changes especially due to the increase in the concentration of gases responsible for the greenhouse effect (CO_2). Such changes cause extreme weather phenomena that increasingly affect pollination periods. Since pollen from the olive tree is one of the principal causes of pollinosis in Madrid we wanted to find out whether climate changes are affecting its aerobiological and clinical behaviour.

Method: Olea pollen counts were carried out between 1979 and 2016 using Hirst volumetric collectors, placed on the roof-top of our clinic. A prevalence study using Skin Prick Tests (SPT) for *Olea europaea* pollen was carried out on our pollinosis patients at the clinic: 1979 (n = 100); 1994 (n = 316), and yearly between 1999 to 2016 (n = 40 998), with an annual average of 2411 patients. The beginning of the season was considered to be the first day of three consecutive days with > 10 grains/m^3 air. The end of the season was considered to be the last day of three consecutive days with < 10 grains /m^3 of air. Data from the Barajas Weather Station was use.

Results: The average five-yearly temperatures were 14.27, 13.88, 14.37, 14.97, 14.28, 14.77, 14.92, and 15.98, which considers a global increase of 1.4°C. The average five-yearly pollen concentrations were 2978, 2341, 3004, 2540, 2236, 2083, 3251 and 2952 grains/m^3. Excellent correlation with temperature (r_s = 0.9, P < 0.05). The annual prevalence of SPT's positive to *Olea* in 1979 was 50%, and in 1994, 61%. The five-yearly averages between 1999 and 2016 were 69, 63, 59 and 60%.

The beginning of the season began 9 days earlier and finished 7 days earlier with respect to the period between 1979 and 1983. The length of the season increased by 2 days.

Conclusion: 1) Temperature increase of 1.4°C in Madrid, over 38 years.

2) No change in Olea pollen count tendencies.

3) Five-yearly variations closely correlated to temperature variations.

4) The season began 9 days earlier and ended 7 days earlier.

5) Discreet increase in the prevalence of sensitization among pollinosis patients in Madrid, shifting from 50% to 60%.

TP1167 | Validation of an in-house monoclonal antibody-based ELISA method for the quantification of Sal k 1 major allergen from salsola kali

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Background: *Salsola kali* belongs to Chaenopodiacea family. Its pollen is an important cause of pollinosis in arid and semiarid areas. Generally, it induces asthma, allergic rhinitis and allergic conjunctivitis in sensitized individuals. The major allergen Sal k 1 is recognized by approximately 67% of the patients sensitized to *S. kali*. Since no commercial kits are available to quantify Sal k 1, our objective was to develop and validate an in-house sensitive ELISA method for its quantification in allergenic extracts.

Method: Three Balb/c mice were immunized with Sal k 1, previously purified from *S. kali* pollen extract by ion exchange and size exclusion chromatography (Laboratorios LETI). After fusion of mouse myeloma and spleen cells, and screening by direct ELISA, several monoclonal antibodies (mAbs) considered positive were purified and tested. Finally, two mAbs that bound two different Sal k 1 epitopes were selected and produced as capture and biotinylated antibodies. ELISA-sandwich conditions were stablished using purified Sal k 1 as standard. Purified Sal k 1 was analyzed by SDS-PAGE and immunoblot and its identity confirmed by mass spectrometry.

For validation of the assay the inter- and intra-assay precision, intermediate precision, linearity/range, accuracy and specificity were determined using *S. kali* pollen freeze-dried samples.

Results: SDS-PAGE and immunoblot analysis of purified Sal k 1 showed a single protein band of approximately 40 kDa, whose identity was confirmed by mass spectrometry.

The ELISA standard curve ranged from 0.488 ng/mL to 1000 ng/mL with a correlation coefficient higher than 0.99, and with a limit of quantification of 7.813 ng/mL. The linearity of the method was tested in the range from 8.21 to 131.4 µg Sal k 1/mg of freeze-dried extract. The accuracy was demonstrated in the same range with a recovery of 93%. Inter- and intra-assay precision and intermediate precision were calculated, being the coefficient of variation of 4.29, 6.93 and 12.43, respectively. Specificity was determined testing *Phleum pratense* and *Alternaria alternata* extracts and showing no Sal k 1 recognition.

Conclusion: The method is considered suitable for the quantification of Sal k 1 in *S. kali* pollen extracts. Particularly, the method has demonstrated to be specific for Sal k 1, to be linear, accurate and precise in the range from 8.21 to 131.4 µg/mg.

TP1168 | Cypress pollen allergy in Georgia

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Background: Cypress pollen allergy is a widely distributed, highly prevalent and severe pollinosis. Cypress trees have a wide geographical distribution and influence the pollen maps of many of the cities. In Mediterranean countries, the cypress pollen is becoming the major source of winter respiratory allergy, commonly inducing symptoms of hay fever, rhino-conjunctivitis, hacking cough, and asthma in sensitized individuals. Depending on the geographic area and studied population, 9% to 65% of outpatients consulting an allergist may have sensitization to cypress pollen. The aim of present study was the evaluation of cypress pollen allergy in Georgian patients.

Method: The airborne pollen monitoring was performed with a Burkard Seven Day Volumetric Spore-trap (Burkard Manufacturing Co Ltd, UK) during pollination period, following the recommendations of European Aerobiology Society. Pollens concentration was calculated and expressed as the number of pollen grains per cubic meter of air (p/m^3). The ImmunoCAP ISAC test was performed according to the manufacturer's instructions (Thermo Fisher Scientific, Uppsala, Sweden) for diagnostic of allergy among outpatients.

Results: According to pollen count data, cypress pollen is the major aeroallergen component in winter and early spring in two main cities (45.2% for Tbilisi and 76.7% for Kutaisi of annual total pollen concentration), which associated with *Cupressus sempervirens*, *Cypress arizonica or Juniperus* from ornamentals in the city's trees and parks. The highest account of tree pollen, about 4471.6 *Cupressaceae* pollen's in m^3 per 24 h (p/m^3), was observed in Kutaisi at the middle of February, in Tbilisi – 4045 p/m^3 at March. Diagnostic results showed that about 25% of patients attending the allergy clinic had positive diagnostic test to cypress pollen. Concerning the clinical expression, rhinitis and conjunctivitis were the most prevalent symptoms, rhinitis 81.4% (95% CI 72.7-87.7%) and conjunctivitis 53.9% (95% CI 44.3-63.3%). Cutaneous symptoms (atopic dermatitis) was recorded only in 3.9% (95% CI 1.5-9.6%) of cypress positive patients and asthma related symptoms was reported in 20.6% (95% CI 13.8-29.4%). Exacerbation during the cypress season was reported in 69.9% of patients with rhinitis, 52.4% with asthma and 9.5% with atopic dermatitis symptoms.

Conclusion: Cypress pollen is the major aeroallergen component and one of the leading causes of respiratory allergy in Georgia.

TP1169 | Can airborne populus seeds be a potential cause of pollen allergies? An aerobiological study

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Background: Poplar female trees produce seeds that have tuft-like trichomes on their outside, which facilitates their transport by wind. These trichomes are composed of cellulose and, although viewed by the population has a cause of respiratory problems, it has been argued that its allergenicity is null. Since these seeds are airborne together with allergenic pollen, we aimed to study if they trap pollen during its dispersion.

Method: The pollen trapped by the airborne Poplar seeds was quantified and compared with the airborne pollen concentrations in the days of the seed dispersal. Individual *Populus* seeds were sampled while in suspension twice a day, pollen was extracted by physical-chemical analysis and quantified using an optical microscope (pollen/mg of sample). Control samples collected directly from the tree were also taken. Airborne pollen was monitored using a 7-day Hirst-type volumetric spore sampler and expressed into morning and afternoon number of pollen grains/m^3. Pearson's and Spearman's correlation coefficients were used to relating airborne pollen, pollen on the seeds, and the meteorological parameters.

Results: In our study, 60% of the 26 different pollen taxa identified on the seed samples are recognized to induce allergic respiratory symptoms, being the most frequent pollen from *Quercus*, Urticaceae, Poaceae, *Pinus* and *Platanus*. In the atmosphere, pollen from Urticaceae, *Quercus* and Cupressaceae were the most representative. The presence of pollen from *Betula*, *Plantago*, *Rumex* and *Salix* was observed. Only significant correlations were found between the meteorological parameters and airborne pollen, pointing out to pollen trapped by the seeds being determined by the different pollen-types atmospheric content.

Conclusion: Airborne Poplar seeds have the ability to scavenge, transport and accumulate pollen in the tuft-like trichomes, which can have a potential impact on pollen allergies if in contact with atopic individuals, when the seeds enter in people's houses, offices and public spaces.

TP1170 | An in vitro exposure chamber for whole pollen at the air-liquid-interface

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Background: Allergy research has entered the fields of detrimental or protective environmental exposure. Most allergies are against pollen. With that comes the need to develop techniques able to get pollen exposure closer to reality. Our aim was to build an in vitro exposure chamber to expose allergy relevant cells at the Air-Liquid-Interface (ALI) to natural pollen in their dry state.

Method: A Pollen Exposure Chamber was fitted inside a cell culture incubator to mimic an epithelial cell environment. Dry and intact pollen were resuspended in air by pressured air. Exposure was tested with birch pollen by counting the amount of pollen per cm^2 on the bottom of the chamber.

A549 and BEAS-2B were exposed at the Air-Liquid-Interface to natural birch pollen at different doses. Total RNA was extracted and Cy3-Microarrays were performed to check for transcriptomic changes on the level of allergy-relevant molecular pathways.

Results: The main problem in the construction of the chamber was the reduction of loss of naturally sticky pollen to the appliance. The next problem was obtaining a low dose of sticky pollen, as in the natural situation. Thirdly, the reproducibility needed to be guaranteed. Different doses of pollen showed a linear increase in deposited pollen. Distribution was homogenous over 6 cell culture wells with a variability of 25 ± 12.5%. We are able to load concentrations of birch pollen close to reality on our Pollen Exposure Chamber, with a loss of pollen to the walls of the chamber of around 38 ± 2.5%. A549 and BEAS-2B did not show cytotoxicity when loaded with birch pollen and the upregulation of allergy-relevant pathways was demonstrated.

Conclusion: The Pollen Exposure Chamber enables exposure of *in vitro* systems to pollen in their dry state at the Air-Liquid-Interface, which mimics the real life allergic reaction. The expression of allergy-relevant pathways proves the utility of this technique for future research on environmental exposures.

TP1171 | Salsola kali sensitization and cross-reactivity with olea europea in patients with pollinosis from Alcázar de San Juan, Ciudad-Real, Spain

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Background: The Allergy Department of Alcázar de San Juan, in the Mancha Centro Hospital (ASJ-MCH), Ciudad-Real, Spain, attends patients with respiratory allergy to pollen of different species, such as *Salsola kali*. Patients mono-sensitive have symptoms in late summer, in the pollination time of *Salsola*, but also in spring, when there is pollination time of other species such as *Olea europaea*. It is described that patients with IgE specific to a single species can recognize epitopes from others by cross-reactivity. In this research we review the cross reactivity between *Salsola kali* and *Olea europaea* in patients from ASJ-MCH.

Method: Skin prick test, sIgE measurements and assessment of allergic diseases were performed in adults attending the ASJ-MCH. Three groups of 4 patients were constituted: G1 - allergic to *Salsola kali*; G2 – allergic to *S. kali* and also to *O. europaea*; G3 – allergic to *O. europaea*. IgE-reactivity patterns of pooled sera from the 3 groups to proteins from *S. kali* or *O. europea* pollen extracts were evaluated by immunoblot. Immunoblotting was also applied to obtain individual allergograms to *S. kali* proteins. Cross-reactivity was assessed by inhibited immunoblotting with *O. europaea* pollen extract.

Results: IgE-reactivity patterns from G1 revealed eleven bands in *S. kali* pollen (9-223 KDa); although G1 was sIgE negative to *O. europeae* pollen, several bands (9-85 KDa) were also detected. G3 sera revealed 17 bands in *O. europaea* pollen (2-160 KDa); Despite being sIgE negative *S. kali*, G3 also identified several bands in this species. In G2, the polysensitized group, many bands from both pollen types were identified, mostly with overlapping MW, suggesting cross-reactivity between *S. kali* and *O. europaea*. Individual IgE-reactivity patterns to *S. kali* showed a band with 40 ± 2 KDa detected by all the patients, probably corresponding to Sal k1 and Sal k 2, and a band with 60 ± 5 KDa detected by 92% of the patients. Bands with 18 ± 1, 14 ± 1 and 12 ± 1 KDa, probably corresponding to Sal k 5, Sal k 4 and Sal k 7, were detected by 58, 50 and 67% of the patients, respectively.

Conclusion: These results suggest cross–reactivity between *S. kali* and *O. europaea* probably as a result of already described panallergens but also of other Sal k allergens. Since both pollen types are highly prevalent in the region, cross-reactivity should be taken into account for individual therapeutic approaches.

TP1172 | The influence of meteorological parameters on intradiurnal patterns of airborne pollen in Helmond, the Netherlands

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Background: A daily pollen forecast is of importance for patients with seasonal allergic rhinitis. Forecast models combine parameters

like the historical pollen count, rhinitis symptoms, field observations and local weather. For the weather, different meteorological parameters (temperature, humidity, rainfall and wind) are included as a daily average. This does not do right to the reality since meteorological parameters change significantly within 24 h. In this study it was investigated if there is a typical intradiurnal pattern for airborne pollen and, if so, how these patterns are influenced by meteorological parameters.

Method: Pollen sampling was carried out in Helmond, the Netherlands using a 7-day recording volumetric spore trap installed at roof level (15 m). Daily samples from selected time periods (1 week in April, June and August from 2012 to 2016) were collected and processed using standardized methods. Hourly counts were obtained by counting the amount of pollen using 1 longitudinal transect. Pollen counts were correlated to the metrological data obtained from a nearby weather station.

Results: Pollen counts per hour fluctuate during the day. For all three time periods there is a tendency for a peak starting in the afternoon to early evening (3-9 PM). Lowest values occurred in the early morning (7-8 AM). Correlations between meteorological data indicated a significant increase in pollen counts if the temperature rises above 20°C, but a significant decrease if the temperature rise further to above 25°C. Rainfall shows a clear, non-significant, negative tendency, while humidity displays a significant negative correlation with pollen counts. Wind also has an impact. For instance, wind speeds above 8 m/s are associated with a lower, non-significant, pollen count. Besides that, wind from the north (northeast to northwest) is significantly correlated with a decrease in pollen counts.

Conclusion: This study shows the intradiurnal variation of pollen counts and how these counts are influenced by meteorological parameters. Based on the preliminary results of this small study, the forecast model in the Netherlands is changed from a daily to an hourly forecast. The coming pollen season the hourly forecast will be validated with actual pollen counts and reported rhinitis symptoms.

TP1173 | Changes in pollen and spore levels during rain and hail

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Background: Pollen and spore expression may be impacted by rain and hail activity.

Method: This study compares atmospheric spore content obtained by two different methods of analysis. Sampling was done by Samplair slit impactor (SAM) and an Anderson N6 single stage viable impactor (AND) all at the same location on the roof of Oliphant Hall at the University of Tulsa (Oklahoma) at an average height of 12 m above ground. SAM and AND samples were collected simultaneously at around 1 PM 3 times per week from December 11, 2017 to April 18, 2018. The AND samples were collected for 2 minutes onto malt extract agar. Culture plates were incubated at room temperature and colonies were identified by microscopy. Colony counts were corrected for multiple impactions; concentrations were expressed as colony forming units (CFU) per cubic meter of air. The SAM was operated for 10 minutes. Bioaerosols were impacted onto a microscope slide coated with Dow-Corning High Vacuum Grease. Samples were stained with a fuchsine-based solution being read with a light microscope. Spore counts were converted to concentrations expressed as spores per cubic meter of air. 48 samples from both were taken during the study period.

Results: On February 23, there was incessant rain and on April 6 sudden hail occurred at the beginning of the regular sampling time. Increased number of both spores and pollen were sampled by SAM during the rain compared with dry conditions. Spore concentration during the hail on April 6 was 11745.87 spores/m, the highest concentration sampled during the study. Spore concentration during rain on February 23 was the 14th highest obtained at 1720.86 spores/m. The lowest spore level occurred before on February 21 at 66.7 spores/m. High pollen levels seen under the hail on April 6 being 8490.91 pollen/m, while on February 23 being 266.8 pollen/m. The highest amount of pollen, 69.9%, sampled on February 23 was Urticaceae pollen, not characteristic of Tulsa, probably brought to the region by a warm air mass from Texas. The number of CFU and culture composition sampled during the rains by AND was: 388.69 CFU on April 6 and 176.68 CFU on February 23, the 23rd and 37th results respectively.

Conclusion: Fungal spore and pollen precipitation processes are impacted by rain and hail perhaps leading to changes in respiratory allergy symptoms in sensitized patients.

TP1174 | Epidemiological study of allergic rhinitis for hospital workers in University of Fukui between 2006 and 2016

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Background: Allergic diseases have been increasing worldwide. The aim of this study was to comprehend trends of epidemiological change in sensitization and prevalence of allergic rhinitis (AR), especially for Japanese cedar pollen (JCP) which is the most common air bourn antigen in Japan and mites.

Method: We recruited 1540 subjects in 2006 and 1498 in 2016 during annual physical examination for workers in our university. Prevalence and sensitization to 7 common aeroallergens in Japan

were measured by means of specific IgE and questionnaire. Those 7 antigens are Cryptomeria japonica (Japanese cedar pollen (JCP), Dermatophagoides pteronyssinus (Der p), Dermatophagoides farina (Der f), Dactylis glomerata, Ambrosia artemisiifolia, Candida albicans and Aspergillus fumigatus) Questionnaire was performed to ask symptoms and diagnosis related to allergic diseases.

Results: Sensitization rate of JCP in year of 20's, 30's and 40's were 59%, 52% and 53% respectively in 2006. Those rates changed to 65%, 64% and 49% in 2016. Sensitization rate of mites of 49%, 40% and 27% in 2006 changed to 46%,49% and 39% in 2016. We found 335 participants who were enrolled in both studies. The remission rate from this group were 13% for JCP, however 36% for mites respectively.

Conclusion: Totally, sensitization and prevalence are increasing; however, pattern of change is not same between JCP and mites. Those lead to different provision for controlling clinical symptoms. The remission rate of JCP is lower than mites, suggesting JCP is more feasible for interventional therapy such as allergen immunotherapy.

TP1175 | The study for revision of threshold levels for pollen allergy risk grade in Korea

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Background: The impact of pollen on human health is primarily evident in allergic diseases. Pollen threshold levels for sensitization are precisely unknown; instead most studies focus on the prevalence of sensitization for different pollen species. The pollen thresholds for symptom development vary among the different studies as well as countries. whereas most of our knowledge on threshold values and symptom development is based on pollen counts in ambient air determined by a pollen sampler in a certain area. But there has been used a risk grade index modified from several countries in Korea and has been needed Korean own threshold level for risk grade. This study was evaluated to revise pollen threshold levels for Korean risk grade recently used for pollen allergy prediction.

Method: Pollens were collected daily from Seoul and Guri as its suburban area by using 7 Day-Burkard sampler (Burkard Manufacturing Co Ltd, Hertfordshire, UK) for 8 years. Oak, pine, birch, Japanese hop and ragweed were selected for study as common pollens in Korea. and Total 1007 Subjects for allergy for those pollens were recruited from Hanyang University Seoul Hospital (n = 248 for Spring, n = 240 for Autumn), and Hanyang University Guri Hospital (n = 258 for Spring, n = 261 for Autumn) for 8 years. Symptom index was evaluated and recorded by phone-calling to study subjects daily or asking allergic symptoms questionnaires when they visit outpatient clinic every week for the evaluation of the relation between pollen concentration and the outbreak of allergic diseases. Statistical analysis of data was analyzed by using correlation coefficients and regression models with time series graph.

Results: Sensitization rates for pollen, especially oak, birch for Spring, and ragweed and Japanese hop for Autumn were increased annually. There are significantly different threshold levels of each pollen between used and revised version of risk grade index. Threshold for risk grade of pollens (oak, birch, pine, ragweed, and Japanese hop) were revised as follows below Table.

Conclusion: There were revised the pollen threshold levels of common allergic pollens for revised results from adjusted symptom index of each pollen allergic patients in Korea. This revised risk grade index for pollen allergy may be very crucial to the prediction model for pollen and be useful to patients with pollen allergy in Korea.

TP1176 | Cross-blocking activity of specific antibodies induced by SLIT with RBet V 1

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Background: We have recently performed a sublingual immunotherapy (SLIT) with the recombinant major birch pollen allergen rBet v 1. Twenty individuals received a daily dose of 25 μg of rBet v 1 and 20 individuals received placebo for 16 weeks. In contrast to the placebo group, Bet v 1-specific IgG4 antibodies rose significantly during SLIT with rBet v 1. Post-SLIT sera from the active group also prevented the IgE-mediated activation of basophils, indicating the induction of Bet v 1-specific blocking antibodies. Various tree pollens contain Bet v 1-homologous major allergens such as Aln g 1 (alder), Car b 1 (European hornbeam), Cas s 1 (chestnut tree), Cor a 1 (hazel), Fag s 1 (European beech), Ost c 1 (hop-hornbeam), Que a 1 (white oak), which through IgE-cross-reactivity may cause allergic reactions in

Risk grade	Oak		Birch		Pine		Ragweed		Japanese hop	
Version	Recent	Revised	Recent	Revised	Recent	Revised	Recent	Revised	Recent	Revised
Mild	0~49	0~2	0~19	0~4	0~499	0~4	0~19	0~4	0~49	0~8
Moderate	50~99	3~11	20~49	5~9	500~999	5~42	20~49	5~9	50~99	9~15
Severe	100~199	12~28	50~99	10~14	1000~1499	43~66	50~99	10~34	100~299	15~32
Dangerous	≥200	≥29	≥100	≥15	≥1500	≥67	≥100	≥35	≥300	≥33

birch pollen-allergic patients. Here, we sought to investigate if SLIT with Bet v 1 induced antibodies that prevent IgE-mediated reactions to these homologous pollen allergens.

Method: First, the IgE reactivity to the different homologs (n = 7) was measured by means of ELISA for each of the individuals before starting SLIT. Then, we tested the presence of IgG4 antibodies against the different pollen allergens by means of ELISA. Currently, we are performing basophil activation tests to assess the blocking capacity of the cross-reactive IgG4 antibodies.

Results: All individuals displayed IgE reactivity to at least one of the homologous pollen allergens; however, the majority cross-reacted with 4 or more allergens. Overall, SLIT with rBet v 1 induced a significant increase of IgG4 against all Bet v 1 homologous pollen allergens except for Car b 1 and Cor a 1. Sera collected after rBet v 1 SLIT inhibited basophil activation with Bet v 1-homologous pollen allergens.

Conclusion: Sublingual immunotherapy with rBet v 1 for 16 weeks induced a significant increase in IgG4 antibodies which cross-react with Bet v 1-homologous pollen allergens with exception to Car b 1 and Cor a 1. Primary experiments provide evidence of a cross-blocking activity of sera collected post SLIT with rBet v 1.

TP1177 | Impact of non-allergenic components of ragweed pollen on IgE synthesis to allergenic components

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Background: This study investigates the role of non-allergenic components of ragweed pollen in modulation of the specific responses to its allergenic components.

Method: Non-allergenic lectin-like substances (LLS) have been isolated from crude ragweed pollen extracts. Allergen-specific IgE antibodies in sera of F1 (CBAxC57BL) mice immunized with the allergen-active fraction (AAF) of ragweed pollen were studied by passive cutaneous anaphylaxis methods. IgE-specific Abs in 7-days culture supernatants of in vitro cultivated mononuclear cells (PBMC) of ragweed sensitive patients were assessed by Phadia CAP assay. The synthesis of IL-1 by mouse peritoneal and splenic macrophages as well as by neutrophils of healthy donors and ragweed-sensitive patients were assayed by ELISA.

Results: Non-allergenic LLS isolated from ragweed pollen induced various immune activities. Intraperitoneal injections of LLS to F1 (CBAxC57BL) mice dose-dependently impacted the synthesis of IgE-Ab to AAF. Simultaneous injections of LLS and AAF stimulated the synthesis of IgE-Ab to AAF, at the same time injections of LLS 24-48 hours prior to immunization with AAF leads to inhibition of the synthesis of IgE-Ab. Co-cultivation of PBMC of ragweed-sensitive patients with LLS and AAF increases the synthesis of IgE. LLS provides multiple immunotropic activities stimulating the production of IgM-PFC more than 1.6- fold; stimulating the phagocytic activity of mice peritoneal and splenic macrophages more than 1.5-fold; and increasing the synthesis of IL-1 by mice peritoneal macrophages as well as by neutrophils of healthy donors and ragweed-sensitive patients.

Conclusion: The existence in extracts, especially in crude forms, of multiple immunoactivity non-allergenic substances may have an impact on the specific response to allergenic molecules used in allergen immunotherapy.

TP1178 | Specificity of mold sensitization among patients with respiratory disease in different settlements in Bulgaria

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Background: It is estimated that approximately 2%-6% of the general population in developed countries is allergic to fungi. In addition, up to 70% of mold-allergic patients have skin test reactivity to *Alternaria*. Studies have demonstrated the frequency of positive skin test varied from country to country. The aim of our study is to asses fungal sensitization among patients from three different settlements (Sofia, Stara Zagora, Krumovgrad). Now we present the data gathered from patients with symptoms of allergy.

Method: Skin tests in 309 patients with following allergen extracts: A1 house dust; A 13- D. Pteronyssinus; EI- Mixed fungal allergen; DII- Mixed fungal allergen; B II Mixed tree allergen; B1 Mixed grass allergen; B29 Mugwort pollen were done. 198 patients show positive skin tests. 111 are negative.

Results: 63 subjects show sensitization to fungal allergens in different combinations: 27- EI- Mixed fungal allergen; 20- E II- Mixed fungal allergen; 16- EI- Mixed fungal allergen and EII- Mixed fungal allergen. 34 patients are sensitized to both seasonal and annual allergens, 38 only to seasonal and 63 to annual allergen. We documented high prevalence of E1 sensibilization among patients in Sofia.

Conclusion: Fungal allergy may vary from settlement to settlement.

TP1179 | A numerical evaluation of cat dander levels by safranin-O staining

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Background: Fel d 1 is the primary allergen responsible for allergic symptoms in people allergic to cats. In cat exposure rooms that

replicate home exposure, Fel d 1 levels can vary greatly over time, making it difficult to predict patient exposure. Quantification of allergen level using ELISA assays are effective but time consuming and delay the ability to regulate allergen levels in a timely fashion. The purpose of this study is to investigate dander counting by staining, light microscopy, and image processing and correlate counts to Fel d 1 levels. This could allow more rapid assessment and tighter allergen level control.

Method: Dander samples were obtained using two different methods. First, cat bedding was shaken vigorously for 1 minute every 15 minutes over 1 hour. Dander was collected by gravity for 15 minutes on isopore and glass fiber filters (Millipore) at 30, 45 and 60 minutes. Second, dander samples were collected for (how much time?) using portable air sampling pumps (Gilian 5000) at 4 L/min using 2 μm glass fiber filters and x mm isopore filters after 30 minutes of dander aerosolization using different aerosolization methods. Fel d 1 collected on glass fiber filters was quantified using ELISA (Indoor Biotechnologies). Isopore filters were stained with Safranin-O (0.01%) for a minimum of 60 minutes and visualized by light microscopy (50 × magnification). Ten images were captured on each quadrant of the filter at different locations. Particle count, area and perimeter of detected particles were obtained by computer analysis using ImageJ Software. From these, the approximate particle diameters, size distribution, and particle densities measured by ratio of particle area to filter area and by count/mm^2 were calculated.

Results: The results obtained from the samples collected by gravity show that the area ratio of particles detected as well as the particle count per mm^2 increased from 15 minutes to 1 hour. A linear correlation was found between Fel d 1 levels and area ratio (R^2 = 0.810). For the dander samples collected using the portable air sampling pumps, a weaker linear correlation was found with a coefficient of determination of R^2 = 0.45.

Conclusion: The results of this study could be useful for the real-time monitoring of allergen concentrations in cat challenge chambers.

TP1180 | Feasibility study: Comparison of source and exposure indexes of allergenic pollen trees in lyon's green spaces with data from the pollen diary (PHD)

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Background: For several years, the number of pollen allergy sufferers has been increasing in France. About 20% of children from 9 years of age and 30% of adults are affected by pollen allergies in France [1]. These pollen allergies (pollinosis) are responsible of many symptoms for sensitive people, like allergenic rhinitis or asthma for the most serious cases. The question of urban green spaces developments is becoming essential, like in the city of Lyon which has different green areas in the heart of the city.

Method: A study was carried out from March to June 2018 on various parks in the city of Lyon in order to help landscape gardeners and local decision-makers for a practice that takes into account the health impact in the choice of species and the maintenance of green spaces. 4 pollen traps were placed in 4 different parks in the city, to analyze the air content of allergen pollen.

In parallel, people allergic to pollens completed a daily pollen diary questionnaire (PHD) on the website: https://www.pollendiary.com/Phd/fr/start. The main points of this PHD concern the area of residence, the general state of health, the types of symptoms and their severity as well as elements concerning the medication taken. An extraction of the data from this PHD for allergic people filling it from March to June 2018 and living in Lyon was carried out to be able to link health impact data and pollen data.

Results: The results obtained following this study enable on the one hand to analyse the pollination periods of the different species, and on the other hand to establish source and exposure indices in order to formulate recommendations to those responsible for green spaces on the species whose establishment in urban areas must be limited. One of the main results of the study is the excessive presence of birch trees in the Erevan garden, as well as historical plane trees all around the Tête d'Or Park.

Conclusion: The RNSA made this feasibility study in order to assess the nature and quantity of pollens that users living in and around these urban green spaces breathe every day and compare them with data from the pollen diary (PHD) completed by allergic people living nearby to determine if allergenic pollen peaks correspond to symptom peaks via the PHD. We need to avoid the local pollen sensitization by stopping planting allergenic species with high allergy potency in green areas and better take in consideration the health impact in the choice of vegetal species to implant.

MONDAY, 3 JUNE 2019
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NEW LABORATORY TESTS AND BIOMARKER CANDIDATES

TP1181 | Demonstration of immunoassay performance of the noveostm specific IgE assay with allergens: D001 (D. Pteronyssinus), E001 (Cat Dander), G006 (Timothy Grass), F013 (Peanut), and W006 (Mugwort)

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Background: Many allergic disorders are mediated by IgE class immunoglobulins. Allergen-specific IgE determinations are valuable tools for the diagnosis and management of allergy. The NOVEOS immunoassay analyzer is a new, high throughput automated platform for the detection of allergen-specific IgE in human serum, and it employs state of the art chemiluminescent, fluorescent and magnetic microparticles technology. To demonstrate the analytical performance of the NOVEOS products, the results from five candidate allergens are presented here.

Method: The NOVEOS sIgE assay precision and functional sensitivity were evaluated in accordance with CLSI EP5-A3 design, and Limit of Blank (LoB) and Limit of Detection (LoD) were determined by following CLSI EP17-A2. Method comparison of NOVEOS and ImmunoCAP sIgE assay results was carried out in accordance with CLSI EP9-A3 and CLSI EP24-A2 using 100 plus specimens per allergen. The assay linearity was assessed in accordance with CLSI I/LA20-A3 and including multiple dilution panels. Exogenous (drugs) and endogenous interferences as well as cross reactivity for the non-IgE immunoglobulin isotypes were assessed in accordance with CLSI EP07-A3 using the pair-difference design.

Results: The NOVEOS immunoassay analyzer demonstrated strong overall repeatability (<12% CV), within-lab precision (<16% CV) across the assay range with all six allergens evaluated. The LoB, and functional sensitivity were determined to be < 0.10 kU/L, and < 0.35 kU/L, respectively. The overall comparison between the NOVEOS sIgE and a commercially available device yield good overall agreement. Clinical sensitivity for each allergen, confirmed either by oral food challenge or skin prick test, demonstrated strong concordance. Assay linearity determined by samples spanning the assay range (LoQ to 100 kU/L) showed good linear regression results across five allergens evaluated. The endogenous (hemoglobin, conjugated bilirubin, unconjugated, triglyceride, IgG, IgA, IgM, and IgD) and exogenous interfering substances (biotin, diphenhydramine, methylprednisolone, and ranitidine) showed insignificant reactivity with the NOVEOS sIgE assay.

Conclusion: The NOVEOS sIgE used in conjunction with capture reagents D001 (*D. pteronyssinus*, House Dust Mite), E001 (Cat Dander), G006 (Timothy Grass) F013 (Peanut), and W006 (Mugwort) demonstrated strong assay performance to aid in the diagnosis and management of allergic diseases.

TP1182 | Evaluation of biotin interference in specific IgE assays processed on the NOVEOS™ immunoanalyzer, Phadia™ 1000 system, and IMMULITE® 2000 instrument

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Background: With the recent emergence of high dose biotin consumption from dietary and beauty supplements, the FDA has issued a safety communication concerning the increased prevalence of inaccurate lab tests caused by biotin interference. According to the FDA communication, such inaccurate results have caused misdiagnosis and, in one instance, death. Diagnostic assays which utilize biotin-streptavidin interaction may be susceptible to elevated levels of biotin in patient serum. This study evaluates the effect of biotin on several allergy diagnostic assays processed on the Phadia 1000, IMMULITE 2000, and NOVEOS platforms.

Method: A panel of patients was selected based on their reactivity of ≥ 0.35 kU/L to allergens D001 (*D. pteronyssinus*, House Dust Mite), E001 (Cat Dander), G006 (Timothy Grass), M006 (Alternaria alternata), and T007 (White Oak). Reconstituted D-biotin was spiked directly into serum at 5 levels from 0 ng/mL to 2000 ng/mL. Samples were then tested on the NOVEOS, Phadia 1000, and IMMULITE 2000 systems and compared against their respective controls.

Results: NOVEOS and Phadia 1000 results showed on average less than 15% bias with all patients retaining their positive value (≥0.35 kU/L). IMMULITE showed significant bias greater than 15% and resulted in all patient samples recovering as negative (<0.35 kU/L).

Conclusion: Although the NOVEOS system utilizes biotin-streptavidin interactions, no significant biotin interference was observed across all levels. NOVEOS results were on par with results from the Phadia 1000 system and suggest minimal potential for biotin interference. The IMMULITE 2000 platform demonstrated significant biotin interference with all patient results, recovering negative even for lowest biotin level tested.

TP1183 | Establishment of an ELISA for quantification of allergen-specific IgE: Comparison with quantitative immunoCAP and chip-based immunoCAP ISAC measurements

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Background: Immediately after the discovery of IgE, quantitative measurements based on the radioallergosorbent assay (RAST) and then ImmunoCAP technology were developed for the measurement of allergen-specific IgE levels. However, the ImmunoCAP technology can only be run on special instruments, consumes rather large volumes of serum and is quite expensive.

Method: In order to establish a standard for the measurement of allergen-specific human IgE, we have expressed and purified a human monoclonal IgE antibody specific for the major birch pollen allergen rBet v 1 (IgEmoAb) and the corresponding allergen. Using IgEmoAb and rBet v 1 we established by ELISA a standard curve allowing to measure and quantify allergen-specific IgE. Using a set of sera from clinically well-characterized birch pollen allergic patients Bet v 1-specific IgE levels were quantified with the IgE ELISA and compared with results obtained by quantitative IgE ImmunoCAP measurements and by ImmunoCAP ISAC chip measurements.

Results: Using IgEmoAb and rBet v 1 we established a standard curve for quantification of allergen-specific IgE with a linear range covering approximately 6 ng/ml to 240 ng/ml. Bet v 1-specific IgE levels determined by the quantitative IgE ELISA correlated well with quantitative IgE levels determined by ImmunoCAP and ImmunoCAP ISAC. The quantitative IgE ELISA can be performed with simple ELISA equipment and requires less than half of the amount of serum required for ImmunoCAP measurements.

Conclusion: We have established a simple quantitative IgE ELISA which allows robust quantification of allergen-specific IgE in the nanogram/ml range. *Supported by a Megagrant of the Government of the Russian Federation, grant number 14.W03.31.0024 and by the "Russian Academic Excellence Project 5-100".*

TP1184 | The first comparison of two multiparameter methods to measure allergen specific IgE among the polish group of kids suffering from allergy

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Background: The diagnosis of allergic diseases faces two major problems. First, a sharp increase in the prevalence of allergy, and second, there are more and more patients for whom it is difficult to establish the diagnosis. There are new, more precise diagnostic tools, such as multiparameter assays, which may be helpful in detection of allergic disease.

Method: Results of sIgE were collected from the Department of Allergology and Pneumonology of the National Research Institute for Tuberculosis and Lung Diseases, Regional Branch in Rabka-Zdrój, Poland performing two multiparameter assays: ImmunoCAP ISAC® and ALEX®. Statistical analysis was done using SPSS programme.

Results: In the our study, 3160 (1580 for ImmunoCAP ISAC® and 1580 for ALEX®) results of sIgE for 79 allergen molecules, which were available on both assays, were analysed for 20 children suffering from allergy. The mean age of children was 7.1 years, with a range from 2 to 16. Three out of four patients were male.

Statistical analysis conducted with Chi-squared test (positive or negative) did not reveal significant discrepancies in the results ($P = 0.104$). The same results on both assays were obtained for 1442 (91.3%) allergen molecules. The concordance rate for negative findings was 70%, whereas for the positive findings – 21.5%. Differences were shown only for 8.7% (138) results for allergen molecules. The outcome of analysis with Spearman's rank correlation coefficient was excellent correlation between the results of ImmunoCAP ISAC® and ALEX® ($P < 0.001$).

The results obtained on both assays were most concordant (100%) for three following molecules: Ara h 9, Bet v 1 and Der p 2. The most clear differences were revealed for molecules: Ara h 1, Cor a 8 (both 75%) and Ara h 3 (55%).

Conclusion: The first comparison of sIgE findings from Polish children suffering from allergy indicated a good correlation between ImmunoCAP ISAC® and ALEX®. There are some discrepancies in the results, and one of this reason, it could be that ImmunoCAP ISAC® is a semi-quantitative test, whereas ALEX® is a quantitative. Although the concordance rate for all findings was satisfying, further research should be done in order to outline the reliability of this new multiplex assay.

TP1185 | A comprehensive comparison between ISAC and ALEX multiplex test systems

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Background: Diagnosis of type I hypersensitivity is based on anamnesis, blood- and skin testing and provocation testing. Multiplex specific (sIgE) testing enables determination of sIgE antibodies against multiple recombinant or purified natural allergen components. The aim of this study was to evaluate the performance of the novel ALEX® (Allergy Explorer) multiplex platform and to compare it with the ImmunoCAP ISAC® test system.

Method: Serum samples of 20 patients, routinely determined with ISAC, were selected based on positive results covering in total 101 of 112 ISAC components. Negative percent agreement (NPA) and positive percent agreement (PPA) of ALEX data compared to ISAC data (as a non-reference standard) were computed for common allergen components (n = 80).

Results: The overall agreement between ISAC en ALEX common allergen components was 92% (both negative (n = 1079) + both positive (n = 395)/1600*100%). The remaining results were ISAC+/ALEX- (n = 61) or vice versa (n = 65). The NPA for a selection of food allergens (egg, milk, storage proteins), inhalation allergens (grass, tree, animals, mites) and cross-reacting allergens (LTP, PR10, profilins) varied between 89%-98%. The PPA was high for inhalation allergens and profilins (91%-100%) and slightly lower for LTP, PR10 and food allergens (68%-88%). Detailed analysis revealed that specific allergen components strongly influenced agreement values. Concerning NPA values, 6 of 6 ISAC-/ALEX+ mite allergen results were positive for Lep d 2 and 3 of 3 ISAC-/ALEX+ grass allergen results were directed against Phl p 6. Moreover, 6 of 13 ISAC-/ALEX+ storage proteins results were positive for Ara h 3. Regarding PPA values, analysis of PR10 allergens showed that 7 of 12 ISAC+/ALEX- results were directed against Ara h 8.

Conclusion: The comparison between ISAC and ALEX sIgE detection against common allergen components showed high overall agreement. Detailed analysis of NPA and PPA values for selected allergen families revealed allergen specific differences between both test systems, possibly reflecting the different methods utilized to immobilize the molecules to different solid-phases.

TP1186 | Molecular profile of patients with allergopathology in different regions of ukraine by the results of ALEX investigation

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Background: Molecular diagnostics is an innovative method of Allergology. Due to different exposure patterns of the patients, their molecular profiles may have regional peculiarities, which are important for choosing the tactics of allergy immunotherapy. Aim. To analyze the profile of patients' sensitization done by Allergy Explorer (ALEX) test for patients from different regions of Ukraine, to find out the possible regional peculiarities of these profiles.

Method: 459 patients aged from 18 to 78 were examined with multiplex allergy diagnostic method ALEX, which was performed in 2018. Among them – 269 women (59%) and 190 men (41%). Distribution of patients by the regions: Kyiv – 45%, Kharkiv – 17%, Dnipro – 18%, Odessa – 8%, Lviv– 7%, other regions – 5%.

Results: Output of component investigations by the regions were following:

Kyiv - Amba 1 (36%), Lolp 1 (30%),Phlp 1 (27%), Betv 1 (24%), Feld 1 (24%), Alng 1 (21%), Derp 2 (18%), Derf 2 (18%),Artv 1 (17%),Alta 1 (10%).

Kharkiv - Amba 1 (45%), Artv 1 (37%), Betv 1 (33%), Derp 2 (31%), Derf 2 (30%),Lolp 1 (26%), Feld 1 (25%), Alng 1 (22%), Canf 1 (20%),Alta 1 (13%)Derp 1 (8%),

Dnipro - Amb a 1 (45%), Fel d 1 (24%),Art v 1 (22%), Bet v 1 (18%), Lol p 1 (17%), Pho d 2 (17%),Phl p 1 (15%), Phl p 12 (14%),Alng 1 (12%), Can f 1 (10%), Alt a 1 (7%).

Odessa - Amba 1 (47%), Derp 2 (22%), Derf 1 (19%), Derf 2 (19%), Alta 1 (19%), Feld 1 (16%), Betv 1 (13%), Artv 1(14%), Lolp 1 (11%)

Lviv - Phlp 1 (36%), Lolp 1(36%),Feld 1 (33%), Derp 2 (29%), Derf 2 (26%),Derf 1 (26%), Derf 23 (22%), Betv 1 (21%),Alng 1(16%),Alta 1 (7%), Amba 1 (5%)

Conclusion: Molecular profile of patients from each region of Ukraine had some peculiarities depending on climatic and geographical location. However, the main cause of sensitization was major allergen of Ambrosia – Amba 1, with the most prevalence in the south of Ukraine (Odessa) and with the least prevalence in western regions (Lviv).

TP1187 | Some trends in the comparative analysis of the results of ALEX in children with allergic diseases

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Background: A comparative analysis of the results of ALEX in children with allergic diseases determines the relationship between the age, the level of total IgE and the frequency of detection of the reaction to allergens and cross-reactive components.

Method: A comparative analysis of the results of ALEX in 98 children with allergic diseases was carried out, taking into account the age, the level of tIgE, the revealed reaction to allergens and the cross-reacting components (CRC) of allergens. There were examined patients aged: 2-4 years - 41; 5-8 years - 33; 9-12 years old - 20; 13-18 years old - 4 children. The examination results were divided according to the level of tIgE (less than 100 kU/L; 100-199 kU/L; 200-299 kU/L; 300-399 kU/L; 400-499 kU/L; 500-599 kU/L; 600 -699 kU/L; 700-799 kU/L; 800-899 kU/L; 900-999 kU/L; over 1000 kU/L; according to the frequency of reactions to identified allergens and CRC of allergens.

Results: The analysis revealed some trends: 1. There is an inverse relationship between the level of tIgE and the age of patients. A low level of total IgE (less than 100 kU/L) was detected in 42% of the examined: at the age of 2-4 years - in 53.7%, in 5-8 years - in 45.5%, in 9-12 years - in 10% (due to a small number the children aged 13–18 years were not analyzed).2. In children with a low level of tIgE (less than 100 kU/L), the percentage of detection of the reaction to allergens increases with age: 2-4 years - 40.9%, 5-8 years - 80%, 9-12 years - 100%. In patients with tIgE levels up to 40 kU/L, the reaction to allergens and CRC was not detected. 3. The frequency of reaction to the cross-reacting components increases with increasing levels of tIgE: up to 400 kU/L in 27.39%; more than 400 kU/L - at 72.00%. At the level of tIgE of up to 100 kU/L, the reaction to CRC was detected only in 14.63% of children. 4. The increased frequency of detection of allergens and CRC is observed in older age groups. The reaction to allergens at the age of 2–4 years was detected in 41.46% of children, at the age of 5–8 years - in 84.85%, over 9 years of age - in 100%. The reaction to CRC in children aged 2–4 years was found only in 26.82%, which is almost 2 times less than in children of other age groups.

Conclusion: Thus, a comparative analysis of the results of ALEX in children showed that there is a certain relationship between the level of tIgE, the age of patients and the frequency of detection of the reaction to allergens and the CRC of allergens.

TP1188 | Application of biochip microfluidic technology to detect serum allergen-specific immunoglobulin E (SIgE)

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Background: Allergic disease is common in both adults and children. Identification of the causative allergens is significant in the disease management and prevention. Meanwhile, specific IgE measurement system with high price performance ratio is lacking in mainland China, especially in the primary care hospitals. The purpose of this study is to evaluate the clinical performance of the BioIC System for multiplexed determination of allergen specific IgE in serum.

Method: sIgE determination was done with the allergen specific IgE assay kit and measured by a chemiluminescence analyzer. sIgE concentration against the following allergens were measured: Der pteronyssinus, Der farinae, Blomia tropicalis, cat dander, dog dander, Bermuda grass, timothy grass, cockroaches, Aspergillus fumigatus, Candida albicans, ragweed, egg white, milk, wheat, peanut, soybean, almond, crab and shrimp.

Results: Totally 293 subjects were found to fulfill the inclusion criteria, with an average age of 23 (range from 8 to 36 years old). Among them, 170 were male and 123 were female. 92 of them had allergic rhinitis, 117 had allergic asthma, 36 with comorbidity of rhinitis and asthma, and 48 had other allergic diseases. Total concordance among Inhalant allergens ranged from 92.00% to 95.33%. For food allergens, the concordance range was 40.74%-72.39%. Highest sensitivity for inhalants was seen in Der farinae

Characteristic	No. (%)
Sex, n (%)	
Female	123 (41.98%)
Male	170 (58.02%)
Age, year, n (%)	
Median (25%, 75%)	23 (8.36)
≤10	97 (33.11%)
11-20	37 (12.63%)
21-40	101 (34.47%)
>41	58 (19.80%)
Diagnosis, n (%)	
Allergic rhinitis	92 (31.40%)
Allergic asthma	117 (39.93%)
Allergic rhinitis with asthma	36 (12.29%)
Others	48 (16.38%)

(93.94%), with 100% specificity. Among food allergens, highest sensitivity was seen in peanut (54.55%), with a specificity of 80.65%.

Consistency analysis for the two systems showed that kappa values for the three inhalants were between 0.727~0.876, with the highest value seen in cat dander as 0.876. They were all better than food allergens which in general fell into < 0.400. Spearman's correlation analysis showed the best correlation was seen in peanut and cat dander, with correlation coefficient as 0.942 and 0.927 respectively. For concordance and discordance analysis, the allergens which showed ± 1 class difference were Der pteronussinus 91.60%, Der farinae 81.25%, cat dander 98.00%, milk 83.58%, shrimp 59.72% and peanut 76.56%.

Conclusion: The current study shows that the two systems demonstrate good consistency. Compared with ImmunoCAP system, BioIC System is easier to use and has a lower demand for operator training. And greatly reduce the set up and running cost and at the same time, which makes the system particularly suitable for allergy screening in primary care hospitals in China.

TP1190 | Does specific IgE to grass pollen allergens/total IgE ratio better reflect the presence of clinically relevant allergy than specific IgE itself?

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Background: We investigated whether specific IgE to grass pollen allergens/total serum IgE ratio better reflects the presence of clinically relevant allergy in sensitized patients than specific IgE to grass pollen allergens itself.

Method: Our study group comprised 34 patients with allergic rhinoconjunctivitis and sensitization to grass pollen. All subjects were examined for total serum IgE (BN II ©, Siemens) and specific IgE to timothy allergenic components Phl p 1 and Phl p 5 by using ImmunoCAP ISAC © (Thermo Scientific). The subjects recorded symptoms of allergy and medication use by mobile application AllergyMonitor© during peak grass pollen season 2018 (May to July). Finally, medians of Rhinoconjunctivitis Total Symptom Score (RTSS) and Average Combined Score (ACS) for every subject and statistical evaluation by using chi-square test were calculated. We aimed to reject the null hypothesis stating that the measured laboratory values do not distinguish between clinically insignificant (RTSS ≤ 1; ACS ≤ 0.583 (for RTSS = 1 and Rescue Medication Score = 1)) and significant grass pollen allergy (RTSS > 1; ACS > 0.583).

Results: 30 enrolled subjects were assessed as they completed the records on more than 50% days in peak grass pollen season. Their median of specific IgE Phl p 1 was 8.07 ISU, the median of specific IgE Phl p 5 was 0 ISU, the median of RTSS was 2, the median of ACS was 0.58. While using cut-off 0.9 ISU for specific IgE Phl p 1 and/or Phl p 5, the null hypothesis could not be rejected both for RTSS ($P = 0.45$), and for ACS ($P = 0.22$). However, while using cut-off 0.05 for the ratio of specific IgE Phl p 1/total IgE and/or specific IgE Phl p 5/total IgE, the null hypothesis was rejected for RTSS ($P = 0.03$), but it could not be rejected for ACS ($P = 0.3$).

Conclusion: The ratio of specific IgE to main allergenic components of timothy pollen to total serum IgE seems to have better capability of recognizing the presence of relevant grass pollen allergy than specific IgE itself. Possibly, future enlargement of our study group might bring stronger evidence for this assumption.

TP1191 | Cross-reactive carbohydrate determinant (CCD) inhibition test can help identify false positive for plant allergen-SIgE caused by CCD

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Background: Pollen allergens are important inhaled allergens and can cause respiratory allergic diseases, especially seasonal allergic rhinitis and asthma. Many pollen allergen and seed have the glycoprotein epitope, the specific IgE (sIgE) tests are often affected by cross-reactive carbohydrate determinant (CCD), cause false-positive reactions. This study analyzed the sensitization of pollen allergens in south China and discussed the effect of CCD inhibitor on the results of sIgE test of pollen allergens. Thus, the objective of this study was to investigate the level and feature of serological IgE cross-reactivity between grass pollen and seed in a cohort of respiratory allergic patients in Southern China.

Method: Two hundred and thirteen patients, with a doctor's diagnosis of allergic rhinitis or asthma, IgE towards at least two common inhaled allergens were recruited. Serum samples were analyzed for IgE against tree mix (willow/poplar/elm Tree), common ragweed, mugwort, humulus scandens, peanut, soy, and cross-reactive carbohydrate determinants (CCD) and specific IgE-binding inhibition experiments were performed.

Results: Among the patients sensitized to multiple allergens, 83 patients (39.0%) were plant allergen sensitization (sIgE positive for any of the above six allergens was defined as plant allergen sensitization, PAS), and 57.8% of PAS patients were positive to CCD-sIgE. PAS subjects were more often sensitized to CCD, known to be cross-reactive between grass and seeds.

CCD inhibited binding to all pollen and seed allergen by 73% to 100% (Table 1). The highest inhibition rate was obtained for Humulus scandens, followed by mugwort and peanut (both 85.2%), common

	CCD pre-inhibited n (%)	CCD inhibited n (%)	Turned rate(%)
Mugwort	27 (81.8)	4 (12.1)	85.2
Common ragweed	27 (81.8)	5 (15.1)	81.5
Tree mix	26 (78.8)	7 (21.2)	73.0
Soy	25 (75.8)	5 (15.2)	80.0
Peanut	27 (81.8)	4 (12.1)	85.2
Humulus scandens	15 (45.5)	0 (0.0)	100.0

ragweed (81.5%), soy(80.0%) and tree mix (73.0%). It was surprised to find that all sIgE against to pollen and seeds from 23 PAS patients were turned to negative after CCD inhibition.

Conclusion: CCD was positive in the serum of most plant allergen-sIgE positive patients in South China. More than 73% plant allergens-sIgE were eliminated into negative after CCD inhibition experiment, suggesting majority the plant allergic patients in southern China, particularly the sIgE against peanut, soybean and pollen allergens, were false-positive caused by the CCD interference. CCD inhibition test should be used in clinical diagnosis, which can help to avoid misdiagnosis of plant allergens.

TP1192 | Identification of unique grass species peptides, in a thirteen grass species aqueous extract sample by LC-MS/MS

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Background: LC-MS/MS is a powerful tool used in proteomics for the identification of proteins by comparing known characteristic peptides against a database. Grass main allergen proteins can have amino acid sequences which are 89% similar and thus provide similar peptides on tryptic digestion. Not all grass main allergens have been thoroughly sequenced or characterised in databases, which makes specific identification only by database searches impossible. Data and methodology is presented for the selection of characteristic peptides to identify thirteen grass species in an aqueous extract for grass, including those with limited or no database sequences.

Method: Method 1, individual and mixed grass species aqueous extract samples were prepared with a standardised tryptic digestion. The resulting complex peptide maps were screened against an in-house grass species specific database created from SwissProt. Database hits were then screened manually for false positives and individuality, to identify unique grass species peptides.

Method 2, Samples of thirteen grass species aqueous extracts were prepared with a standardised tryptic digestion. The resulting complex peptide maps were screened manually against the identified unique peptides in method one to identify unique peptides across the thirteen grass species. These were then used to confirm the presence of grass species in blinded samples containing up to thirteen different grass species.

Results: Method 1, multiple unique peptides for grass species were identified for seven of the thirteen grass species (*Holcus lanatus*, *Poa pratensis*, *Secale cereal*, *Festuca pratensis*, *Lolium perenne*, *Dactylis glomerata* and *Phleum pratense)* via database and manual screening. The six grass species for which unique peptides were not identified (*Cynosurus cristatus*, *Alopecurus pratensis*, *Arrhenatherum elatius*, *Anthoxanthum odoratum*, *Bromus inermis* and *Agrostis capillaris)* are not sufficiently characterised in databases.

Method 2, multiple unique peptides for grass species were identified for the remaining six species (*Cynosurus cristatus*, *Alopecurus pratensis*, *Arrhenatherum elatius*, *Anthoxanthum odoratum*, *Bromus inermis* and *Agrostis capillaris)* not identified above. Thirteen grass species were identified using the unique peptides in blinded samples.

Conclusion: In depth screening of peptide maps by LC-MS/MS can be used to identify thirteen grass species in a complex mix via unique peptides.

TP1193 | Characterization of a panel of profilin allergens for a structure-based IgE-epitope mapping

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Background: Panallergens frequently cause respiratory allergy and oral allergy syndrome. Profilins are important panallergens because of their highly conserved structure and ubiquitous presence in allergy sources. Therefore, determination of the structure and biophysical characterization are important tasks to complement IgE-binding studies and enable structure based epitope prediction. In this project six recombinantly produced profilins will be used for structural characterization and experimental determination of cross-reactivity between important respiratory and food allergens. The examined profilins are the food allergen Cuc m 2 (melon – Cucumis melo) and Cit s 2 (orange – Citrus sinensis), the pollen allergen Ole e 2 (olive tree – Olea europaea), Fra e 2 from

the European ash (Fraxinus excelsior) and Phl p 12 (timothy grass - Phleum pratense) as well as the storage mite allergen Tyr p 36 (Tyrophagus puturescentiare).

Method: All allergens were produced in *E. coli*. Biophysical characterization including Circular Dichroism spectroscopy, Differential Scanning Fluorimetry and Size Exclusion Chromatography are used to prove the allergens' native state. Crystallization and homology modeling coupled to bioinformatics provide structural information and IgE-binding assays immunological data on cross-reactivity.

Results: All six profilin allergens included in this study were recombinantly expressed and purified to homogeneity. Biophysical characterization revealed the structural integrity of the allergens and their monomeric state, which makes them well suited for immunological testing. Homology modeling elucidated the surface-accessible regions of the allergens.

Conclusion: Immunological data regarding cross-reactivity in combination with structural information will enable more accurate IgE-epitope predictions using a structure based IgE-epitope mapping approach (Dall'Antonia et al., 2011) for the profilin family of allergens.

TP1194 | Investigations of the major horse allergen Equ C 1 derived from the presumably hypoallergenic curly horse

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Background: The horse breed American Bashkir Curly horse is claimed to be hypoallergenic due to reports of allergic patients experiencing fewer symptoms while handling this special breed. Recently published results demonstrate neither reduction in allergen content in hair extracts from Curly Horses nor a reduced allergen release into the air compared to other horse breeds.

Objective: To investigate if alterations in allergenicity and amino acid sequence identity of the major horse allergen Equ c 1 purified from Curly Horses could provide an explanation for reduced symptoms in horse allergic patients.

Method: Native Equ c 1 was purified from hair extracts prepared from a male and a female Curly Horse, a male Tinker horse and a mix of hair extracts from 193 individuals of different breeds and gender. Purification was performed by affinity chromatography with HiTrap NHS-activated HP column coupled with Protein G affinity purified polyclonal antibodies raised against recombinant Equ c 1. Native Equ c 1 was examined by SDS-PAGE followed by silver staining and mass spectrometry. The allergenicity of native Equ c 1 from all sources was assessed by ELISA using 10 sera of patients allergic to horse dander.

Results: Native Equ c 1 purified from extracts of different breeds has the same molecular weight. SDS-PAGE followed by silver staining shows a major band at approximately 28 kDa and a minor band at 35 kDa. Patients' sera had similar IgE titers to all native Equ c 1 samples with medians from 15.57 kU/L (Equ c 1 mix from 193 different breeds) to 20.44 kU/L (Equ c 1 from the male Curly Horse). Mass spectrometry revealed 3 different variants of Equ c 1 that were found in every sample. No differences in the amino acid sequence between Equ c 1 from male Tinker horse, male Curly Horse and female Curly Horse were observed. The relative concentrations of the 3 variants differed greatly between male and female Curly Horse, but not between the male Curly Horse and the male Tinker horse.

Conclusion: IgE titers of horse allergic patients do not differ between major horse allergen Equ c 1 purified from Curly Horses and Equ c 1 purified from other breeds. These results give no evidence for an altered allergic response from patients to the major allergen from this breed. Mass spectrometry confirms the existence of 3 different Equ c 1 variants whose relative concentrations may depend on gender rather than breed.

TP1195 | Identification and characterization of a novel allergen, 30 KDa lipoprotein, from silkworm pupa

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Background: Silkworm pupa is widely consumed in Asian countries and allergic reactions after ingestion have been described. However, false-positive responses of skin prick test or specific IgE responses to total extract of silkworm pupa make diagnosis difficult. This study aimed to identify allergens from silkworm and evaluate their IgE reactivities.

Method: A novel IgE reactive protein, 30 kDa lipoprotein, was identified from silkworm pupa by a proteomic analysis. Recombinant protein was overexpressed in *Escherichia coli*, and purified by affinity chromatography using Ni-resin. IgE reactivity of recombinant proteins was compared by ELISA with the other allergenic proteins: arginine kinase (Bomb m 1), 27 kDa glycoprotein, tropomyosin, and 30 kDa lipoprotein.

Results: Recombinant 30 kDa lipoprotein was recognized by IgE antibodies from all 17 sera from allergy patients, whereas IgE binding frequency for the other proteins were 35.3% (6 of 17) for 27 kDa glycoprotein, and 0% for arginine kinase and tropomyosin. IgE reactivity increased significantly, especially for 30 kDa lipoprotein, when urea was added to denature the protein structure in serum samples for ELISA, indicating that linear epitopes play a major role for IgE recognition.

Conclusion: A novel allergen 30 kDa lipoprotein displayed a strong IgE reactivity. Recombinant allergens produced in this study may facilitate the development of better allergy diagnostics for silkworm allergy.

TP1196 | Betula verrucosa may be taken as a marker allergen for Tx5 tree mix

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Background: Allergen extract mixes are commonly used in routine allergy diagnostics. The aim of the study was to investigate if one or several tree pollen allergen extracts of the IDS Specific IgE assays (formerly Allersys®, Omega Diagnostics) give similar results to the ImmunoCAP® mix tx5. Tx5 contains Hazel and Grey alder which are known to have IgE cross reactivity between them as well as to Common Silver birch. Tx5 also contains extracts from Elm, Willow and Cottonwood that are rarely prevalent in Northern Europe.

Method: 30 samples from a biobank containing serum from Northern European routine patients were tested simultaneously on the ImmunoCAP tx5 mix, the tree pollen extracts included in tx5 (*Alnus incana*, *Corylus avellana*, *Ulmus americana*, *Salix caprea*, *Populus deltoides*) and ImmunoCAP MUXF (cross reactive carbohydrate determinants, CCD). On the IDS system, samples on *Alnus incana* and *Corylus avellana* were tested. The allergen *Betula verrucosa* Was included additionally on both systems.

Results: 10/12 samples negative on tx5 (<0.35 kUa/L) were also negative on all allergens tested across both platforms and on MUXF. 2 samples negative for tx5 had positive sIgE for Birch, the 2nd sample also for Alder and Hazel. Positive samples for tx5 (n = 18) had detectable sIgE mainly for Alder, Hazel and Birch on both assays, with Birch showing the highest concentration. SIgE for Willow and Cottonwood was positive in 3/18, and for Elm in 5/18 samples. There were 2/18 positive tx5 samples that gave a positive MUXF response. 1 of these showed a similar concentration for all tree pollen allergens on ImmunoCAP suggesting that the positive result may be due to anti-MUXF sIgE. The MUXF-positive sample was negative for the 3 IDS tree pollen allergens.

Conclusion: Positive results for tx5 were due to Alder and Hazel allergens in the mix for this population. There was a high concordance between tx5 positive results and the individual Birch assay. It is possible that any of these 3 single allergens could be an alternative for tx5. SIgE for Elm, Willow, Cottonwood was rarely detected in tx5 positive samples. One sample was negative in tx5 but positive for single tree allergen assays across both platforms. Conversely, 1 sample that was positive in tx5 and in all single ImmunoCAP assays was negative in all IDS assays. This sample gave a positive result in the MUXF assay, suggesting that there are differences between the IDS and ImmunoCAP assays relating to interference by CCD.

TP1197 | Phleum pratense may be taken as a marker allergen for Gx3 grass mix

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Background: Allergen extract mixes are commonly used in routine allergy diagnostics. The aim of the study was to investigate if one or several allergen grass extracts of the IDS Specific IgE assays (formerly Allersys®, Omega Diagnostics) give similar results to the ImmunoCAP® mix gx3. All grasses of the ImmunoCAP mix gx3 belong to the Pooideae family and are known to have IgE cross reactivity. Phl p 1 and Phl p 5b are recommended as genuine markers for this grass family.

Method: 30 serum samples from a biobank containing specimens of routine patients were tested simultaneously on the ImmunoCAP gx3 assay, on the grass allergen extracts included in the gx3 mix (*Anthoxanthum odoratum*, *Lolium perenne*, *Phleum pratense*, *Secale cereale*, *Holcus lanatus*) on both the ImmunoCAP and IDS assays. In addition, samples were tested on the component mix rPhl p 1, rPhl p 5b on both platforms. All samples were also tested using ImmunoCAP MUXF. 420 tests were performed.

Results: All samples were negative (<0.35 KUa/L) in the MUXF assay, ruling out that any response was due to cross reactive carbohydrate determinants (CCD). All samples with values < 0.35 kUa/L for the gx3 grass mix (recommended cut-off) also had negative sIgE on the single grass allergen extracts and on the rPhl p 1/ rPhl p 5b mix on both platforms. One sample that gave a positive value (0.43 kUa/L) in the gx3 assay was found to give responses ranging from 0.17 to 0.33 kUa/L with the ImmunoCAP single grass allergens and a value < 0.1 kUa/L in the ImmunoCAP Phl p 1/5b assay. In contrast, values in the IDS specific IgE grasses and in the IDS Phl p 1/5b assay were < 0.1 kUa/L. The skin prick test result for this patient was negative using grass pollen.

Conclusion: All samples measured with ImmunoCAP gx3 mix showed concordant results to all of the reflexed grass extracts (ImmunoCAP) suggesting high cross-reactivity. *Lolium perenne*, *Phleum pratense and Holcus lanatus* showed the best agreement to gx3. The IDS *Phleum pratense* showed the best concordance to the ImmunoCAP gx3 mix suggesting that IDS *Phleum pratense* may also be an alternative for gx3 in this patient cohort. Component testing was useful to confirm genuine sensitisation. There was potentially a false positive result in the ImmunoCAP gx3 assay confirmed by negative results in the individual grass allergen assays, the component mix and clinical information. Further studies with higher samples numbers need to confirm *Phleum pratense* as a marker allergen for gx3.

TP1198 | Analytical performance of a new chemiluminescent singleplex IgE assay

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Background: The correct determination of allergen-specific and total IgE concentrations is essential in allergy diagnosis. We aimed this study at testing the analytical performance of a new chemiluminescent IgE immunoassay.

Method: NOVEOS™ is a singleplex IgE chemiluminescent immunoassay (HYCOR Biomedical, Inc., Garden Grove, CA, USA) using streptavidin-coated magnetic beads, a biotinylated capture allergen, and monoclonal anti-human IgE antibody. We examined the test's analytical performance by measuring, in sera of allergic patients, the concentration (expressed in kU/L) of IgE antibodies to the extracts of *Dermatophagoides farinae*, cat dander, timothy grass and peanut. Analytical sensitivity (limit of blank [LoB] and limit of detection [LoD]), linearity, interfering substances (methylprednisolone, diphenhydramine, omalizumab), intra- and inter-assay 5-day precision, comparison vs WHO calibration, total time to first result (TTFR) and hands-on time were examined and compared to internationally acceptable criteria (I/LA20, 3rd ed, 2016).

Results: LoB and LoD were 0.03 kU/L and 0.08 kU/L, respectively. Linearity of the 4 allergens ranged between R^2 = 0.9909 and R^2 = 1 (ordinary least square regression analysis). Interference by methylprednisolone, diphenhydramine and omalizumab had spiked recoveries <±15%, Intra- and inter-assay 5-day precision gave acceptable results for all levels tested. The correlation of the calibration method to WHO calibrator was high. The TTFR ranged between 105 and 107 minutes. Hands-on time ranged from 97 to 124 minutes.

Conclusion: The NOVEOS specific IgE assay presented a good analytical performance, with results falling within the CLSI and I/LA20 criteria. We are now testing the clinical validity of this novel IgE assay in populations of allergic patients.

TP1199 | Method development for allergen capture from allergenic sources using human IgE-antibodies

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Background: The titration of specific serum IgE is an important biomarker in clinical diagnosis and management of allergic patients. Component-resolved approaches based on single allergen components increase the sensitivity and the specificity of in-vitro testing. However, available allergen panels are limited to known allergen components. We thought to develop a new immunoassay for the capture of novel allergens from allergenic sources using IgE-antibodies from allergic patients.

Method: IgE-Aviquant, a chimeric construct composed of the FcεRI ectodomain and an avian IgY constant domain, was produced in HEK293 cells and purified by column chromatography. The purified antibody was bound to epoxy Dynabeads, followed by coating of variable amounts of IgE-antibodies from sera of food-allergic patients (peanut, fish). Purified allergens were bound to IgE ligated to the IgE-Aviquant/bead-construct. Eluted allergens were quantified by allergen-specific ELISA and identified by mass spectrometric (MS) analysis.

Results: The IgE-binding capacity of IgE-Aviquant, as determined using an anti-chicken IgY ELISA, was shown to be variable depending of the nature of individual patient sera. Bound IgE-antibodies varied in a range from 2000-5000 ng per co-immunoprecipitation assay. Allergens (peanut, fish) were bound in a range between 3.8-6.0 nmol per assay, depending on the allergen-specific IgE-sensitization profile of the index patient serum used. Eluted allergens were quantified by ELISA, recovering expected amounts as calculated for antibody/antigen-binding rates. MS analysis of allergen eluates confirmed the presence and identity of the applied food allergens.

Conclusion: We established a co-immunoprecipitation assay, based on a chimeric construct binding IgE from allergic patients, which allows specific binding and elution of allergens. This assay provides the basis for capturing new allergens from any allergen source for their future characterization and application in diagnostic settings.

TP1200 | Periostin forms the complex with IgA in human serum

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Background: Periostin binds to several integrins on cell surface, playing important roles as a matricellular protein for the onset of allergic inflammation. Since periostin expression is induced by IL-4 and IL-13, serum periostin is expected to be a novel biomarker for diagnosis and prognosis, and a predictive marker for biologics by reflecting type 2 inflammation in allergic diseases. We previously showed that most serum periostin exists as an oligomeric form, but it remains obscure how periostin forms the complex. In this study, we sought to learn how periostin forms the complex in serum, whether the periostin complex in serum is functional, and whether the complex formation interferes with the reactivities to anti-periostin antibodies.

Method: To identify composition of the periostin complex in human serum, we purified the periostin complex from human serum by immunoprecipitation and then applied it to the LC/MS analysis. We examined whether mouse periostin forms the complex with IgA as well as human periostin and whether the periostin/IgA complex is formed in IgA-lacked human serum. We evaluated the function of serum periostin complex by the cell adhesion assay to integrin $\alpha_v\beta_3$. Moreover, we compared the reactivities of several anti-periostin monoclonal antibodies recognising each domain of periostin to recombinant periostin or the periostin-IgA complex purified from human serum by the surface plasmon resonance assay.

Results: We found that periostin forms the complex with IgA1 by the ratio of 1:1. Periostin composing the complex in serum contained at least five different isoforms of periostin. However, IgA is not essential for the oligomeric formation of periostin in mouse serum or in IgA-lacked serum. The periostin-IgA complex in human serum was functional sustaining an ability to bind to $\alpha_v\beta_3$ integrin on cell surface. Moreover, all of the domains except the R4 domain would broadly contribute to the formation of the complex with IgA so that the reactivities of anti-periostin antibodies recognising these regions were interfered.

Conclusion: Periostin forms the complex with IgA in human serum. The complex of periostin and IgA is functional sustaining an ability to bind to $\alpha_v\beta_3$ integrin; however, formation of the complex interferes the reactivities of anti-periostin antibodies.

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NEW LABORATORY TESTS AND BIOMARKER CANDIDATES

TP1201 | Sublingual immunotherapy in patients with perennial allergic rhinitis and SCUAD phenotype

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Background: An important subpopulation in perennial allergic rhinitis (PAR) is represented by polysensitized patients with moderate to severe form of disease inadequately controlled by drug treatment according to generally accepted guidelines. Most of these patients are unsatisfied with pharmacological therapy (PhT) and belong to severe chronic upper airway disease (SCUAD) phenotype. We evaluated in real-life clinical practice the effectiveness of sublingual allergen immunotherapy (SLIT) added to PhT in polysensitized PAR patients unresponsive to drugs.

Method: The prospective (randomized and controlled) study covered 16 adolescent and adult subjects, aged 14-55 years with moderate to severe PAR with/or without allergic asthma, induced by hypersensitivity to different (grass and/or ragweed) pollen and Dermatophagoides pteronyssinus, with poor answer to PhT and indication to SLIT. The experimental group was composed of 9 patients subjected to perennial SLIT (antiallergic biologically standardized vaccine in the form of oral lyophilisate (Dermatophagoides pteronyssinus extract) and PhT, while 7 adequate matched patients on PhT only served as controls. Clinical effects of SLIT was evaluated by the PAR symptom-drug (diary card) score (SDS) measurement, visual analogue scale score (VAS) measurement (control of PAR), severity of PAR measurement (according to ARIA guidelines) and nonspecific bronchial hyperreactivity (NBH) measurement (methacholine bronchial provocation test) before initiation of SLIT and 1 year later.

Results: The SDS were significantly reduced in patients subjected to SLIT ($P < 0.01$) 1 year after the onset it. VAS also was significantly reduced ($P < 0.05$) with satisfied control of PAR and the same time with translation from moderate-severe to mild-moderate PAR, after SLIT. We did not observe any significant changes in the NBH, 1 year after the onset SLIT. In patients receiving PhT only, SDS, VAS and severity of SAR did not change and significantly higher ($P < 0.01$) from the value obtained in the experimental group. NBH also remained unchanged and significantly higher ($P < 0.05$) then in experimental group.

Conclusion: Perennial SLIT added to PhT shows short-term beneficial clinical effects in polysensitized patients with PAR and SCUAD phenotype.

TP1202 | Immunological assessment of different allergen-specific immunotherapy types in children with hay fever

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Background: the aim of our clinical study was assessment of immunological changes in comparative research of sublingual (SLIT) and subcutaneous (SCIT) immunotherapy in children with pollinosis.

Method: 110 children aged 5-18 years with diagnosed pollen sensitization were enrolled in our study during 2013-2017 years. Molecular allergo-diagnostic tests with recombinant allergens were used in patients with multiple sensitizations. ECP concentration in blood serum and nasal secret was determined for disease severity assessment. Total serum IgE and allergen specific IgE, IgG_4 antibodies were measured. Treatment safety was estimated according to the frequency of local and systemic reactions.

Results: Our results showed that among major inhalant recombinant allergens the highest sensitization rate belongs to Art v1-Art v3– in 31 (46.3%), followed by Art v1 in 10 (14.9%) and Art v 1,3-Bet v1, Art v 1,3-Phl p1,5 in 9 (13.4%) patients. ECP level positively correlated with the intensity of nasal inflammation $r = 0.71$ ($P < 0.001$). The level of total serum IgE significantly decreased in both study groups. Likewise, there was a reverse correlation between specific IgE and IgG4 level. Undesirable local and general reactions occurred in 2 times frequently in 40 (85.11%) of SCIT group compared to 26 (41.27%) of SLIT patients.

Conclusion: recombinant allergens determination is an important tool for hay fever diagnosis. Complex comparison of the effectiveness and safety of two different immunotherapy types showed that SLIT is a reliable and safe method in children with multiple sensitizations.

TP1203 | Objectivation of the deviation of the natural course of patients with asthma and rhinitis in specific allergen immunotherapy with dermatophagoides and blomia

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Background: Allergen-specific immunotherapy (IT) can modify the natural course of allergic diseases, efficiently reducing symptoms

and the need for pharmacological treatment. The objective of this study was to evaluate the deviation of the natural course of respiratory allergies in patients who are being treated with specific allergen IT for *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, and *Blomia tropicalis*.

Method: The improvement of patients with asthma and rhinitis, was evaluated using symptom score and standardized treatment scales (ACT, GINA and PCSM); with a follow-up time of seven IT periods. The geometric mean, the median and the interquartile range (IR) were applied. To compare the scores, the Friedman test and a mixed model of repeated measures as a method of adjusting variables was used.

Results: A total of 34 patients were evaluated with a median age of 13 years (IR = 6). Patients had an average of 28 immunotherapies, with a treatment time of approximately 30 months. Directly proportional changes between the compliance time in the IT and the ACT score were observed; moreover, changes inversely proportional to the scores of the PCSM and GINA scales, these effects on the scores were statistically significant ($P < 0.0001$).

Conclusion: Considering the three most important species of sensitization to mites *D. pteronyssinus*, *D. farinae*, and *B. tropicalis*; the continuity of the allergen-specific IT with mites, significantly improves the health status of sensitized patients, diverting the natural course of the disease.

TP1204 | An accelerated build-up phase increases the adherence to allergen subcutaneous immunotherapy. A retrospective study

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Background: Since commuting to receive the injections for subcutaneous allergen immunotherapy (SCIT) is one of the main reasons for poor treatment adherence, it has been suggested that abbreviating the build-up phase, therefore reducing the number of injections, is a way to improve patients compliance.

Method: An abbreviated build-up with a hypoallergenic allergoid pollen preparation has already demonstrated to be safe and feasible. To verify the impact of this schedule on patients adherence, we retrospectively analyzed sales data of the manufacturing Company to backtrack how many prescriptions each patient admitted to the abbreviated schedule has received; we compared these data with adherence of patients treated with the same allergoid product, but with the standard 7 injections pre-seasonal schedule. While "adherence" to SCIT is not a standard defined concept, we considered the number of patients treated for at least two years, the number treated for at least three years and the number of drop outs after one-year treatment only.

Results: The survey included 139 patients, 75 males and 64 females, mean age 35.9, treated with different pollen extracts starting at least 3 years ago. The adherence to SCIT was compared to that of a sex age matched group of 302 consecutive patients, treated with grass extract in the same period. 89.9% of patients treated with the abbreviated schedule completed at least 2 years treatment, while 64.7% continued up to 3 years. By contrast, in the control group the adherence to treatment after two years was only 52.6% ($P = 0.0001$), and it decreased to 26.8% after three years ($P = 0.0001$). Furthermore, the dropout rate in the control group after one year was 46.4%, while in the abbreviated group was 10.1% ($P = 0.0001$).

Conclusion: These data confirm that shortening the treatment schedule with allergoids extracts significantly increases patients adherence, thus improving clinical benefits and at the same time reducing the waste of healthcare resources.

TP1205 | Early efficacy of double-species mites allergen immunotherapy in allergic rhinitis

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Background: An increase prevalence of allergic rhinitis (AR) was found in the recent years, which seriously affects the quality of life of patients and increases their economic burden. Patients usually co-sensitized with Der p and Der f. This study aimed to evaluate the early efficacy of standardized double-species mites allergen immunotherapy (DM-AIT) in AR.

Method: This was a prospective study enrolling 63 AR patients received subcutaneous immunotherapy with mixed preparation of Der p and Der f (1:1). Visual analogue scale (VAS) rhinoconjunctivitis quality of life questionnaire (RQLQ), serum specific IgG4 (sIgG4), basophil activation test and skin prick test (only followed up at V0 and V2) were serially followed up at baseline (V0), the completion of initial treatment (V1) and the first-stage of maintenance treatment (V2).

Results: 14 patients were lost during followup, corresponding to the dropout rate of 22.22%. Compared with V0, the VAS and RQLQ assessed at V1 and V2 were significantly decreased (presented as median with the order of V0-V1-V2, similarly hereinafter, VAS:

23.00-11.00-10.00, RQLQ: 48.50-27.00-22.00) ($P < 0.001$). The median score in specific VAS and RQLQ were as followed: sneeze (5.00-3.00-2.00), rhinorrhoea (5.00-3.00-2.00), rhinocleisis (5.00-3.00-2.00), rhinocnesmus (5.00-2.00-2.00), eye symptom (3.00-2.00-1.00), and activity (6.00-4.00-3.00), sleep (4.00-2.00-1.00), general problems (11.00-7.00-5.00), practical problems (7.00-5.00-4.00), nasal symptoms (10.50-6.00-5.00), ocular symptoms (4.50-2.00-1.00), emotions (6.00-3.00-3.00). The median levels of sIgG4 to Der p were significantly higher than those in the previous stage (14.21-38.43-76.20, mgA/L). The skin wheal indexes of Der p and Der f at V2 were significantly decreased, while no remarkable change was found in the percentage of peripheral blood basophil activation.
Conclusion: Standardized DM-AIT could significantly alleviate the symptoms of patients with AR, improve the quality of life, induce the production of protective antibody sIgG4 and reduce skin reactions early.

TP1206 | Effectiveness and safety of allergen-specific immunotherapy in allergic rhinitis and asthma patients: Experience of a Portuguese immunoallergology department

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Background: Allergic rhinitis and asthma appear as conditions with great impact on life quality, being a significant cause of absenteeism. Allergen-specific immunotherapy (ASIT) has arisen as an effective and widely used therapy on nasal and bronchial symptoms control as an add-on treatment.
Method: Consultation of medical records of six or more year aged-children, teenagers and adults with diagnosed allergic rhinitis and/or asthma, evaluating the effect of ASIT on symptoms control and in reducing the need for medication, after a minimum three years period under this therapy.
Results: A total of fifty patients met the criteria mentioned above, in whom 54% (n = 27) were male; mean age was 23.8 ± 11.8 years (minimum: 11; maximum: 56). In majority (n = 30; 60%), rhinitis and asthma coexisted. Most patients were sensitized to grass pollens (n = 33; 66%). In forty-four patients (88%), the initial route of administration was subcutaneous. The mean duration of treatment was 3.69 ± 0.56 years (minimum: three; maximum: five). No statistically significant differences concerning number of sensitizing agents ($P = 0.1$) or baseline IgE ($P = 0.9$) were found between groups of longer (four or more years) and shorter (less than four years) treatment duration. Among patients with longer treatment we found coexistence of asthma and rhinitis. One third of patients with previous non-controlled disease(s) (n = 18) did not need pharmacotherapy anymore and nearly forty percent (n = 7; 38.9%) became asymptomatic in a year of conclusion of therapy. In patients with previous partially controlled condition(s) (n = 32), we found twenty-eight patients (87.5%) becoming asymptomatic or only reporting symptoms sporadically. They were not found predictive factors of a better response. Six patients reported local pruritus in subcutaneous route of administration; no other adverse or fatal events occurred.
Conclusion: In this sample, significant improvements in symptom control and reduction of medication needs were achieved with ASIT, with an reasonable safety profile. These data are concordant with recent evidence upon clinical benefit of ASIT. In future, it would also be interesting to evaluate the long-term maintenance of ASIT clinical effects in these patients.

TP1207 | The effects of sublingual immunotherapy in our department

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Background: The sublingual immunotherapy (SLIT) may be the only therapeutic method that can treat a symptom of allergic rhinitis by inducing immunotolerance. In Japan, we can use SLIT for Japanese cedar pollen from 2014. We verify the effects of SLIT so far.
Method: We have 30 patients who have been treated their Japanese cedar pollinosis by SLIT from 2014 to 2018.
Although most of them continue their treatment for years, a few patients stopped their treatment by the reason of their work.
In the patient who could continue their treatment, we examined the effect of SLIT.
Results: There is an age limit for SLIT from 12 to 64 in Japan, and we do not start SLIT from February to May because of Japanese cedar pollen season.
23 patients continue SLIT and they do remedy almost every day.
Although 3 patients take antihistamine and/or use nasal spray with steroid during pollen season, most of them are not take any medicine.
Young patients (especially junior high school students) may realize the effect earlier than elderly patients. We think that young patients can be managed by their parents, and rarely forget to take medicine.
There is no serious complication in our department.
Conclusion: We have now small number of patients and want to accumulate a case in the future. We think that we may have a good treatment result so far.

TP1209 | Comparative analysis of sublingual immunotherapy medicines for adherence and clinical outcomes

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Background: Sublingual immunotherapy (SLIT) is a recently introduced immunotherapy using mouth floor mucosal immune system. It has been known to be effective in reducing symptoms of allergic rhinitis (AR) and safer than subcutaneous immunotherapy. *The purpose of this study was to compare the adherence, efficacy, and side effects of SLIT medicines: SLITone®, Lais®, and Staloral®.*

Method: Fifty three patients suffering from AR symptoms and sensitized only to house dust mite allergens were enrolled in this study from January 2000 to December 2015. We investigated demographic data, treatment duration, dropout rate, and adverse events. The visual analogue scale (VAS) including sneezing, rhinorrhea, nasal obstruction and itching were scored from 0 (normal) to 10 (severe), before and after SLIT. Dropout rate was defined as the number of patients who discontinue SLIT of oneself compared to the number of patients who receive SLIT.

Results: Mean age, sex, and mean treatment duration of enrolled patients were not statistically significant among three groups. Total symptom scores were significantly decreased in SLITone®, Lais®, and Staloral® (all $P < 0.001$). Furthermore, there was significant difference in efficacy between SLITone® and Staloral® group. Four patient out of 26 in SLITone® group, 4 patients out of 30 in Lais® group, and 11 patients out of 26 in Staloral® group have stopped SLIT of themselves. Therefore, dropout rate of SLITone®, Lais®, and Staloral® group was 15.4%, 13.3%, and 42.3% respectively. Only 1 patient complained adverse reaction such as swelling of mouth floor in Staloral® group.

Conclusion: Although all three SLIT medicines are effective in improving AR symptoms, the dropout rate was the highest in the Staloral® group. Therefore, we should consider the medication adherence when prescribing SLIT medicines, especially Staloral® for successful treatment outcomes and reducing the possibility of relapse.

TP1210 | Clinical and immunological changes after 1-year treatment with a tyrosine-adsorbed mite allergoid: D. Pteronyssinus 50% + D. Farinae 50%

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Background: A standardized allergen extract from *Dermatophagoides pteronyssinus*, chemically modified into allergoids with glutaraldehyde and associated with microcrystalline tyrosine (MCT) as a depot aluminium-free adjuvant, showed a good tolerability and effectiveness in previous studies. The aim of this study was to generate real-world evidence for the same product with a mixture of *D. Pteronyssinus + D. farinae*.

Method: Ten adult patients with allergic rhinitis, with or without asthma, caused by house dust mite (HDM) were treated for 1 year with a glutaraldehyde-modified MCT-adjuvanted *D. pteronyssinus - D. farinae* 50-50% allergen preparation manufactured by Allergy Therapeutics (Worthing, UK). Combined symptom-medication score (CSMS), daily symptom score (dSS), daily medication score (dMS), rhinitis control, ARIA classification, symptoms intensity assessed by patients on a visual analogue scale (VAS) and serum specific IgE and IgG4,) before and after immunotherapy were compared.

Results: Ten patients (4 women, 6 men; mean age 35 years) were assessed. All patients had persistent rhinitis (disease duration average 12.3 years) and 3 of them also had asthma (disease duration 7 years). The results before and after 1-year treatment were: CSMS (2.6 vs 0.5); dSS: (1.33 vs0.39); dMS: (1.27 vs 0.11); ARIA classification (100% of patients with persistent rhinitis before immunotherapy vs 100% of patients with intermittent rhinitis after immunotherapy; 90% with moderate-severe rhinitis before treatment vs 100% with mild rhinitis after treatment); rhinitis control (100% of patients with partially controlled rhinitis before immunotherapy vs 100% with controlled rhinitis after immunotherapy). VAS (6.15 vs 0.5). At comparing clinical parameters before and after immunotherapy, all the differences were statistically significant ($P < 0.05$). Immunological tests showed significant changes in specific IgG4 (0.52 mg/L vs 0.85 mg/L), not observed in specific IgE levels (27.8 kU/L vs 30.2 kU/L).

Conclusion: Specific immunotherapy with an allergoid of *D. pteronyssinus + D. farinae* 50-50% associated to MCT in patients allergic to *HDM* leads significant improvement in clinical and immunological outcomes in real-world practice.

TP1211 | Effectiveness of sublingual allergen-specific immunotherapy (ASIT) in patients with adverse gastrointestinal reactions in the course of the therapy

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Background: The sublingual ASIT found use as a viable and effective method of therapy. Patients demonstrate high compliance to the treatment. Though, sometimes it causes the gastrointestinal adverse reactions which results in refusal of treatment by patients. Typically, in such situations patients are attempted to switch to subcutaneous ASIT. This method has restrictions particularly in pediatric population.

Method: In this article we present our successful experience in maintaining the sublingual mode of ASIT in 5 patients: two adults and 3 kids (5-8 years old, male and females). All the patients were given ASIT with the birch pollen allergen. The sensibilization profiles of the patients were confirmed by presence of specific immunoglobulins E (IgEs). During the sublingual ASIT abdominal pains of various intensities were registered in all the patients. However, medical screening did not reveal any pathological changes in gastrointestinal tract. All the patients and caregivers gave written informed consents for the ASIT.

In the course of the ASIT treatment at the point where the maintenance dose had been established moderate abdominal pains without oral allergic syndrome emerged within 30 minutes to 2 hours after taking the allergen. All the patients stated willingness to continue the treatment. Therefore, the traditional therapy regiment of sublingual ASIT were modified. The following therapy regiment were proposed: after a two-week interval the course of ASIT was resumed as 1 puff in the morning the dosage 10 IR/mL with the dose escalation every other day by 1 puff until the maximum tolerated. The maximum dose remained the same during two weeks and was taken every other day. And then an attempt to increase the dose was undertaken. If the pain syndrome reappeared the previous treatment was returned. We were able to attain the medicine level as high as 1-2 puffs with the dosage of 300 IR/mL.

Results: Children were treated in the course of one year and showed a significant clinical effect which was decreased symptoms during the pollen season. Adults received ASIT according to the proposed therapy regiment more than a year with a high effect.

Conclusion: The proposed scheme is not a universal one and considering a small quantity of our patients further clinical corrections are needed. However, our experience demonstrates the fact that the adverse gastrointestinal reactions could not serve as an absolute contradiction to sublingual ASIT.

TP1212 | Parallel combination of AITs in a teen-age boy

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Background: We demonstrate a case report of a teen-age polysensitised but also polyallergic and polysymptomatic boy treated with combination of AITs parallelly.

Method: 14- years old boy suffering from allergic rhinitis and allergic persistent asthma due to allergy to house dust mites (spec IgE Der. pteronyssinus > 100 U/mL, Der.farinae > 100 U/mL) as well as birch pollen (spec IgE Bet v 1 > 100 U/mL) was treated in our office. There were also other allergens relevant – grass pollen (spec IgE Ph p 1 = 32.8 U/mL), cat (spec IgE Fel d 1 = 5.7 U/mL). The worsening of asthma occured in the same quality and quantity during autumn, winter and spring.

Results: We started SLIT Staloral 300 100% house dust mites in August and the successful initiation of this AIT was followed with parallel SCIT Pollinex Tree in December. Nowadays our patient has undergone this combination of AITs for three years. His symptoms did ameliorate together with his spirometry, FeNO. We could reduce his antasthmatic and antirhinitic medication.

Conclusion: This case report is only one small evidence of the parallel administration of two AITs in polyallergic and polysymptomatic patient. This combination improved the patient's quality of life and enabled the step-down in his therapy. We continue the follow up of this patient.

TP1213 | Sublingual immunotherapy with 5-grass pollen extract tablets: Can immunization to cross-reactive non-specific lipid-transfer proteins (NsLTPs) occur?

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Background: Non-specific lipid-transfer proteins (nsLTPs) are the most prevalent plant-food allergens in Mediterranean countries, in particular in many vegetables and fruits that are part of the Mediterranean diet. They have also been identified as major and minor allergens in various botanical families, such as Poaceae (in particular Zea mays and Triticum aestivum). The clinical pattern of LTP-allergy may include symptoms that range from local oropharyngeal symptoms up to anaphylaxis and may be influenced by co-factors such as exercise, heat, alcohol intake, strong emotions and non-steroidal anti-inflammatory drugs (NSAIDs).

Multiple sensitization to plant-food and pollens has been reported as LTPs are also important allergens in pollens.

Method: Ten female patients, aged between 19-30 years old, came to our observation with a positive history for adverse plant-food

reactions and rhinitis. Diagnosis was confirmed by positive prick skin tests to grass pollens and prick-to-prick tests with fresh fruit and vegetables, and subsequently, with the detection of anti-LTP specific IgE antibodies. We treated these patients with 5-grass (dactylis glomerata L; anthoxanthum odoratum L.; lolium perenne L; poa pratensis L; phleum pratense L) pollen tablet sublingual immunotherapy for seasonal allergic rhinitis. The first administration took place under medical supervision in a hospital setting and none of the patients presented adverse reactions. We advised patients to eat only plant-foods of the Mediterranean diet, containing also nsLTPs which had not caused any adverse reaction thus far. In addition, we advised patients not to use NSAIDs concomitant to food intake and not to practice exercise in the 4 hours following meals.

Results: All patients presented improvement of nasal/ocular symptoms and reduction of the use of symptomatic drugs during the pollen season treatment with once-daily sublingual immunotherapy of 5-grass pollen tablets, over a 2-year period and tolerated the ingestion of plant foods containing nsLTPs.

Conclusion: On the basis of our observation, and through careful clinical management, we suggest that pollen immunotherapy may have a protective role in nsLTP allergy. Further studies are needed to explore the possibility of desensitization in nsLTPs allergy.

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IN VIVO AND IN VITRO TESTS FOR ALLERGY DIAGNOSIS

TP1214 | Could multiple allergen simultaneous test detect the additional allergen sensitization and improve allergic rhinoconjunctivitis diagnosis?

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Background: Skin prick test (SPT) and serum ImmunoCAP specific IgE are frequently used in the evaluation of allergen sensitization; however, in clinical practice, primary physicians prefer multiple allergen simultaneous test (MAST) because it provides various allergen test results. We aim to evaluate whether the utilization of MAST improves the detection of other aeroallergen sensitization and the diagnosis of allergic rhinoconjunctivitis (ARC) by comparison with ImmunoCAP or SPT using common 6 aeroallergens.

Method: SPT and ImmunoCAP for common 6 aeroallergens (*Dermatophagoides farina* (*Der f*), cat, dog, alternaria, birch, and Japanese hop) and MAST for 33 aeroallergens including the 6 aeroallergens were analyzed simultaneously in 480 children. ARC was diagnosis by the ISAAC questionnaire. We measured the agreement between the SPT, ImmunoCAP, and MAST with Kappa value, and area under the curve (AUC) diagnosing ARC.

Results: The number of children with positive SPT, ImmunoCAP, and MAST results regarding 6 aeroallergens were 258 (53.8%), 314 (65.4%), and 291 (60.6%), respectively. When all 33 aeroallergens were examined by the MAST, the number of subjects with positive results increases to 312 (65.0%). Twenty-two subjects (5.8%) showed negative ImmunoCAP, but were found to have sensitization by the MAST. Seventy five subjects (15.6%) showed negative ImmunoCAP, but were found to have sensitization by the SPT. The kappa values for the agreement between SPT and MAST and ImmunoCAP and MAST were 0.606 (95% CI 0.536-0.693) and 0.737 (95% CI 0.674-0.800), respectively. The area under the ROC curve for allergic rhinoconjunctivitis by sensitization according to SPT, ImmunoCAP, and MAST were 0.640 (95% CI 0.587 – 0.693), 0.640 (95% CI 0.588 – 0.692) and 0.664 (95% CI 0.613-0.715), respectively. When targeted on 33 aeroallergen, the area under the ROC curve decreased to 0.655 (95% CI 0.604-0.706) but no statistical difference ($P = 0.335$).

Conclusion: The MAST does not improve diagnosis rate of ARC; however, it may be used as a supplementary test to SPT and ImmunoCAP in the measurement of aeroallergen sensitizations.

TP1215 | Outdated allergen extracts have equivalent potency and bioavailability as unexpired extracts for the detection of allergen sensitization by skin testing

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Background: The expiration date of drugs is determined by the drug manufacturers to assure the efficacy and safety of the drug. However, several studies indicate that under certain conditions, many drugs have an extended shelf life that lasts years after the original expiration date. Allergen extracts that are used for detection of allergen sensitization have short shelf lives that, together with their relatively high price, limit their use by those who can't afford it. We hypothesized that the in vivo efficacy and bioavailability of the outdated reagents will have a much longer activity than labeled and that they will be useful for the diagnosis of allergens in suspected allergic individuals.

Method: We enrolled 34 participants with allergic rhinitis and 5 participants with Hymenoptera hypersensitivity who had positives skin testing. After confirming allergen sensitization with the unexpired extracts, each participant had a second skin test, performed within 30-60 minutes, with the outdated one (up to 7 years post-expiration date). All the outdated extracts were from the same company and storage at the same conditions as the unexpired one. All extracts were tested for microbiological contamination before use. The results of the skin tests were compared between unexpired and outdated extracts for each participant. The trial was approved by the Helsinki committee from our center.

Results: There was no bacterial or fungal contamination in extracts. All outdated extracts produced a positive wheal reaction of more than 3 mm, with an average of 8.1 mm (range 4-12) that was not significantly different than the unexpired allergens average of 8.7 mm (range 5.3-12.1), and compared to histamine wheal average of 5.8 mm. Seven years outdated lyophilized Hymenoptera extracts showed no significant differences in wheal's size intradermal skin test reactions at 1 mcg/mL, being between 7-10 mm (mean 8.4) and 5-9 mm (mean 6.8 mm) for outdated and unexpired, respectively.

Conclusion: Outdated allergen extracts are safe and have equivalent potency and bioavailability as unexpired extracts for the detection of allergen sensitization by skin testing. These results support our hypothesis that allergen extracts have a longer efficacy and bioavailability than the original expiry date labeled by the manufacture's

company and that for diagnosis of aeroallergens and Hymenoptera sensitization, the use of outdated allergens can be extended after the expiration date.

TP1217 | Evaluation of autologous serum skin test positivity and autoantibodies status in patients with chronic spontaneous urticaria (CSU)

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Background: About 50% of patients with chronic spontaneous urticaria (CSU) have functional autoantibodies against IgE receptors or against IgE bound to their receptor on cutaneous mast cells, and these can be evaluated in vivo using the autologous serum skin test (ASST). Positive ASST is associated with a more severe condition and presence of other positive autoantibodies, such as anti-thyroperoxidase (TPO). The aim of this study was to evaluate whether patients with CSU associated or not with the presence of autoantibodies, such as antithyroid and antinuclear factor (ANA), had a higher TSA positivity.

Method: The medical records of patients with a diagnosis of CSU without associated thyroid disease, who were followed up at a tertiary center and who had performed the TSA were evaluated. Anti-TPO, anti-thyroglobulin (Tg) and ANA autoantibodies (AA) were evaluated. Patients were classified as positive AA (CSUAA+) and negative AA (CSUAA-). Demographics, frequency of angioedema (AE), refractoriness to antihistamines (AH1), and ANA pattern, when positive, were evaluated.

Results: Seventy-four patients participated in the study, being 91.9% female, with an average age of 49.1 years, age of onset of CSU of 34.3 years and time of CSU of 15.1 years. Forty patients (54.1%) had AA, of which 74.4% had ANA, 55.3% anti-TPO and 42.1% anti-Tg positivity. The distribution of ANA titers was as follows: 1/80 - 34.5%, 1/160 - 41.4%, 1/320 - 13.8% and 1/1280 - 10.3%, being the fine speckled nuclear pattern the most common in 48.3% of cases, followed by homogeneous nuclear pattern in 20.7%. There was no difference on urticaria time, AE frequency and AH1 refractoriness between groups. The UCEAA + group had a higher frequency of TSA positive (45.0% vs 32.4%).

Conclusion: This study observed that patients with CSU and the presence of anti-thyroid autoantibodies and/or ANA had a higher TSA frequency than patients with CSU and AA negative. ANA was the most frequent AA.

TP1218 | An nasal secretion preparation method: Paving an effective way for noninvasive local IgE measurement

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Background: Serum antigen specific immunoglobulin E (sIgE) is integral for the diagnosis of allergic rhinitis (AR). However, the role of nasal local inflammation has been ignored during AR diagnosis.

Method: Patients with nasal symptoms were divided into house dust mite (HDM)-IgE$^+$ and HDM-IgE$^+$ group. Nasal secretions (NasSecs) were collected using sinus package in different materials PVA, PVF, PVAc and cross-linked PVA. Antigen-specific IgE to HDM Derp 1 and Derp 2, inhalant antigen were measured in serum, nasal secretions and concentrated nasal secretion of the same patient.

Results: The area under ROC curve (AUC) score of sIgE indicated that PVF (0.8085) for nasal secretion collection is better that the other materials PVA (0.7681), PVAc (0.6747) and cross-linked PVA (0.7742). Additionally, the concentration process improved the specificity and sensitivity of the sIgE measurement in the nasal secretion. Especially, the AUC score increased from 0.8085 to 0.9135 in PVF group after concentration, and the same effect of concentration was also observed in other groups.

Conclusion: This is the first study to standardize the nasal secretion collection method. We have demonstrated for the first time the concentration process facilitates the sIgE measurement in nasal secretion especially using PVF material. The combination of antigen specific IgE measurement in Serum and local nasal secretion will help us better understand the pathogenesis of AR.

TP1219 | IgE testing in nasal secretions

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Background: The analysis of nasal secretions (NS) of patients with allergic rhinitis (AR) permits to provide valuable information about the immunological reaction to allergens at the target organ. In a collaborative study, we have previously shown that IgE antibodies to mite allergens can be reliably demonstrated with microarrays in NS of adult patients with mite allergy and chronic rhinosinusitis. Objective of the study was to investigate with a microarray technology the repertoire of specific IgE (sIgE) antibodies in nasal secretions of patients with seasonal allergic rhinitis (SAR).

Method: Nasal secretions were collected with an absorbent device (Merocel 2000®, Medtronic)from 161 Italian patients with SAR and diluted with saline solution. The levels of (B) Total protein (PierceTM, Thermo Scientific),(C) total IgE (ImmunoCAP, Thermofisher), (D) sIgE antibodies (ISAC-112, Thermo Fisher) were measured and their actual values corrected for the dilution factor. Total and allergen specific IgE were also measured in the patients' sera.

Results: The NS samples had the following mean values: (A) volume = 643 µl; (B) total protein concentration = 3.6 mg/mL; (C) tIgE = 35.7 kU/L; (D) cumulative specific IgE antibodies = 18.9 ISU. Phl p 1 was the molecule most frequently recognized by IgE (47.2% of the 161 NS samples), followed by Phl p 5 (32.9%). The average concentration of sIgE against individual major allergenic molecules ranged from 0.6 to 4.0 ISU. The level of cumulative specific IgE antibodies detected in the NS were strongly related in each patient to the total IgE level in the NS themselves. The detection of IgE antibodies to a given molecule in the NS predicted with a high specificity the presence of those antibodies in the patient's serum.

Conclusion: Testing nasal IgE to allergen molecules predicts with high specificity the sensitization profile in the serum. The hypothesis, that NS can be used as a surrogate of the patient's serum in the diagnostic work-up of pollen allergy, needs further investigation.

TP1220 | The correlation between nasal eosinophil count and percentage in children with allergic rhinitis

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Background: Allergic rhinitis is the most common atopic disease and the most common chronic disease of children. Eosinophil count and percent in nasal smear are useful for differential diagnosis of allergic rhinitis. There are studies for nasal eosinophilia in allergic disease. However, the basis of these criteria is not sufficient. There is a lack of research on the eosinophil percent in nasal smear. Also, there has been no study of whether the eosinophil counts and percentages in nasal smear are related. The aim of this study is to investigate the correlation between nasal eosinophil count and percent.

Method: Between January 2017 and August 2018, 221 children patients with a clinical history of rhinitis were tested at the outpatient respiratory and allergy unit of the department of pediatrics, school of medicine, the Catholic university of Korea. Nasal secretion was collected by swabbing 3~4 times a children's nasal inferior turbinate with a cotton swab. And then placed on to a glass slide. Later, the smear was stained by Giemsa stain. All specimens were examined by the same blinded microscopist, without knowing the clinical histories. Usually the test is done on that day.

Results: This study is the first to assess the comparison of nasal eosinophil count and percent. There is a positive correlation between nasal eosinophil count and percent Y = 1.0195 X + 2.8201 (Y = Eosinophil count, X = Eosinophil percent).

Conclusion: The cutoff value is based on nasal eosinophil count 10 / HPF or nasal eosinophil percent 10%, In patients with suspected rhinitis, one of the values of nasal eosinophil count or percent can be estimated clinically.

TP1221 | Local specific immunoglobulin E in rhinitis and local nasal response in Russian population

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Background: Several studies demonstrate the importance of local specific immunoglobulin E (sIgE) measurement as a new approach for diagnosing rhinitis patients either with or without atopy. We also consider nasal mucosa a target organ responsible for the primary contact with different aeroallergens. The contact could cause local sensitization and immune response. We have checked the approach in Russian population.

Method: Nasal samples from 110 patients with clinical symptoms of rhinitis were tested. 43 children at the age of 5 to 18 and 67 adults from 19 to 67 were included in the study. 18 samples were obtained from patients with suspected local allergic rhinitis (LAR). All 110 samples were obtained via mucosal brush biopsy of the inferior turbinates. Local total IgE production and specific IgE production were evaluated. ImmunoCap tests for house dust mix (hx2), molds and yeasts mix (mx2), tree pollen mix (tx9), weed mix (wx2), animal protein allergen mix (ex2) and grass pollen mix (gx1) were performed.

Results: ImmunoCap test results of 0.35 kUA/L and higher were considered positive. Control group results were lower than 0.35 kUA/L. Hx2 positive results were in 72, 7% of tested samples. Mx2 tests were positive in 58, 2% of nasal samples. Animal protein allergen mix tests ex2 were positive in 91, 8% of tested nasal samples. Tree pollen mix tx9 tests showed positive results in 65, 5% of cases. Weed mix tests were positive in 91% of tested nasal samples. Grass pollen mix gx1 tests showed positive results in 33, 6% of tested samples. 68.2% of all tested patients had polyvalent sensitization. 65, 1% of children had polyvalent sensitization. Total nasal IgE concentrations varied greatly from 0.56 to 71.32 IU/mL. Median total nasal IgE level was of 6.03 ± 9.13 IU/mL. LAR was confirmed in 12 of 18 patients (66.7%). Among LAR patients 7 showed sensitization both to seasonal and perennial allergens. 3 patients with LAR were sensitized to seasonal allergens and 2 patients to perennial.

Conclusion: Local specific IgE measurement via ImmunoCap in samples obtained by mucosal brush biopsy of inferior turbinates could be an easy diagnostic approach to evaluate local immune response.

TP1222 | Results of nasal provocation test, change in patients with systemic or local allergic rhinitis, according to visual analog scale vs rhinometry

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Background: Nasal provocation test (NPT) is the gold standard to evaluated allergic rhinitis. The aim of this study was to evaluate the NPT with *D. pteronyssinus*, using two differences evaluation scales and compared the results in patients with systemic and local rhinitis.
Method: Subjects were assigned to control group or to one of the rhinitis groups (rhinitis with systemic IgE sensitization or rhinitis without IgE systemic sensitization). NPT was considered positive either with a change in the visual analog scale (VAS change ≥ 5 points) or rhinometry (change > 25% in the minimum cross-sectional area). The prevalence ratio (PR) among the study groups was applied.
Results: The mean age of subjects in the three groups was 29 years, an 60% were women. The diagnostic accuracy in the control group (negative NPT) was equal with rhinometry and VAS (80% respectively) (concordance 86.67%). In patients with rhinitis and systemic atopy, the diagnostic accuracy was better for the rhinometry result (84.21%) compared with VAS (73.68%) (concordance 89.47%). The rhinitis group without systemic IgE sensitization presented better diagnostic accuracy with VAS (87.5%) than with rhinometry (68.75%) (concordance 56.25%). Other atopic comorbidities (asthma PR 2.1, dermatitis PR 1.9, and conjunctivitis PR 2.3) were associated with increased risk of chronic rhinitis with systemic atopy, when compared with rhinitis patients without systemic IgE sensitization ($P < 0.05$).
Conclusion: The NPT is a useful instrument for the diagnosis of systemic and local allergic rhinitis. However, we observed important differences in the results, according to the evaluation scale in patients with systemic or local IgE sensitization.

TP1223 | Prediction of positive nasal provocation test according to molecular components of furry animals

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Background: Sensitization to allergen components has been linked to rhinitis, but there are few studies evaluate their relationship with respiratory diseases using objective measures like nasal provocation test.
Objective: To evaluate the prevalence of IgE sensitization to allergenic components from cat, dog, and horse and their relationship with nasal provocation test (NPT).
Method: Dander extract and sIgE levels to pets components (Can f 1, Can f 2, Can f 3, Can f 5, Fel d 1, Fel 2, Fel 4 and Equ c 1) were measured in a rhinitis group (n = 101) and a control group (n = 68). Nasal challenge test was done in patients with IgE sensitization to pets.
Results: Dog and cat dander sensitization were frequent among rhinitis and no-rhinitis subjects. Sensitization to dog (29.7% vs 20.5%) and cat (18.8% vs 8.8%) components was higher in the rhinitis group but it was only statistically significant for cat ($P = 0.05$). Polysensitization for dog or cat components was the principal predictor factor for a positive NPT with each one. Additionally, positive NPT with one animal, increase the risk of sIgE sensitization and positive NPT to the other. Five patients were sensitized to horse and two of them had a positive NPT.
Conclusion: Sensitization to pets dander identify most atopic patients, but its utility to predict clinical relevance is unclear. Allergenic components could help to define the clinical relevance of sensitization to furry animals and could reduce the need for provocation test.

TP1224 | Phenotypes diagnosis of allergic rhinitis using nasal provocation test

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Background: Nasal provocation test (NPT) with an allergen allows to evaluate the reaction not only in the shock organ, but also on the mucous membranes in general. *Aim of study*: to develop and describe a method for diagnosing neutrophilic, basophilic and eosinophilic phenotypes of allergic rhinitis (AR) by conducting a NPT with a allergen and determining the increase in tryptase, myeloperoxidase(MPO) and eosinophilic cationic protein(ECP) levels in nasal lavage and oral fluid.
Method: In 30 patients with AR and 20 healthy volunteers before and 30 min after the NPT with Dermathophagoides pt. determined the result by estimating the release of MPO from neutrophils, tryptase from mast cell and basophil, ECP from eosinophils in nasal lavage, oral fluid
Results: NPT with a minimally selected concentration of allergen(by dilution skin test) did not cause the development of clinical symptoms, but allowed to verify the response of the nasal mucosa to an allergen intake. After a NPT, 27 (90%) patients with AR showed a significant increase in tryptase level after 30 min ($P = 0.043$) in contrast to healthy volunteers. The diagnostic criterion for an increase in the level of tryptase was 7.8 pg/mL (according to ROC). After the NPT, it was revealed that 53% of patients with AR experienced a significant increase (over 16%) of MPO in nasal lavage ($P = 0.03$). In 23 (76.6%) patients with AR, a positive increase in the level of ECP was detected. Before provocation, the

level was 829.9 [673.3; 986.6] pg/mL, and 30 minutes after it was 1080.9 [896.6; 1265.3] pg/mL, $P = 0.001$. The level of eosinophilia in smears imprints most correlated with the level of eosinophilic cationic protein ($R = 0.62$).An increase in biomarkers in nasal lavage and oral fluid when an allergen is exposed to a shock organ (nasal mucosa) confirms the involvement of mast cells, eosinophils and mucosal neutrophils in the allergic process. There was not the growth in the control.

Conclusion: Pathogenetic mechanisms of allergy are polymorphic. The results demonstrate the diagnostic potential of NPT with an allergen. These correlations of increased biomarkers in nasal lavage and oral fluid after NPT confirm the idea of a single mucosal immunity. The developed NPT with the determination of biomarkers in nasal lavage is a method for diagnosing neutrophilic, basophilic and eosinophilic phenotypes of AR.

TP1226 | Different phenotypes of the sensitization in allergic respiratory patients

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Background: Allergic rhinitis (AR) is a symptomatic disorder characterized by immunoglobulin E (IgE)-mediated reaction due to inflammation of the nasal mucosa after allergen exposure. The duration and severity of AR are affected by numerous factors such as genetics, environmental factors, exposure time and exposure amount. The aim of this study was to evaluate symptom severity assessed by ARIA criteria and by virtual scale (VAS) in a group of patients with sensitization to one or more allergens.

Method: 135 patients (58 males and 77 females, mean age 40, sd 16 years) were enrolled in the study. Inclusion criteria was the documented diagnosis of sensitization to common pneumoallergens (house-dust mite, molds, epidermal animal, tree pollen, weed pollen, grass pollen). The individual profile of phenotypes in these patients was evaluated by fluoroimmune assay.

Results: The analysis showed that poly-allergic patients are characterized by a median number of 4 allergens. The median of VAS was higher in polyallergic than in patients with sensitization to one allergen in the subgroup of patients with non seasonal allergy (median 6 (IQR 4.5-8) vs 4.5(IQR 1-6), $P = 0.039$).

Conclusion: The present study confirms the link between allergy and phenotype, showing a different phenotype if the patient is mono or poly-sensitized.

TP1228 | Toward identifying biomarkers of efficacy of allergen immunotherapy

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Background: Allergen immunotherapy (AIT) is an attractive therapeutic option as it may change the natural history of the disease. In many patients with a positive skin prick test it is difficult to predict the benefit of a AIT based only on the symptoms at presentation- the effect can only be evaluated after four months of treatment. In this study we performed conjunctival provocation test (CPT) and basophil reactivity and sensitivity to house dust mite (HDM) tablet (12 SQ-HDM). In 12 consecutive patients with rhinitis due to mite allergy likely to receive SLIT with HDM tablet to determine the range of responses to treatment drug.

Method: 12 patients (age 20-55, 9 women) visiting Allergy Center, Aarhus University Hospital, with clinical symptoms of rhinitis and skin prick test > 3 mm and elevated sIgE > 0.35 to mite allergens, were considered to receive Allergen Immunotherapy. A basophil activation test (BAT) and a diagnostic CPT were performed to assess the reactivity to HDM tablet.

Results: All patients had clinically relevant mite allergy. The CPT was positive at between 1000 and 30 000 SQ-U/mL. Basophil reactivity ranged from 17% to 89%, and sensitivity ranged from 4.5×10^{-3}– 75 SQ-U/mL. (16500-fold). There was no correlation between concentrations at which CPT was positive, basophil reactivity and basophil sensitivity.

Conclusion: There is wide variation in all assessed parameters, and none are clear candidates as biomarkers of allergen immunotherapy.

TP1229 | Elucidating the role of platelet functions in the development of severe allergic reactions

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Background: Allergic diseases and their severity has significantly increased in the developed world, so there is a need to improve the classification and treatment of allergic patients. A recent study of our group pointed out platelets as key players in profilin-mediated food allergic patients with severe reactions. Our aim in this work was to validate platelet-related genes as potential biomarkers in other severe allergic phenotypes such as allergic patients to olive pollen.

Method: 16 subjects were classified in 3 groups, according to their clinical history: non-allergic (n = 6), mild (n = 5) and severe (n = 5). RNA extraction was performed on ficoll-isolated PBMCs using the RNeasy® Mini Kit (Qiagen) and its quality was assessed with Experion RNA StdSens analysis kit (Bio-Rad). For gene expression profiling, we used GeneChip® Human Gene 2.1 ST Arrays (Affymetrix, Santa Clara, CA, USA). R 3.5.1 was used for data analyses. Data normalization and differentially expressed genes identification were performed with *oligo* and *limma* package. Pathways and gene regulators involved in this allergic process were identified using several public databases such as KEGG, Reactome and DAVID. Gene Set Enrichment Analysis (GSEA) was also performed. Finally, results were validated by quantitative real-time PCR (qPCR).

Results: Principal component analysis (PCA) depicted a good separation of the 3 phenotypes. Moreover, mild patients and healthy subjects showed a similar expression pattern while severe patients were completely different. In line with previous findings, pathways involved in inflammatory response, histone modifications, platelets and coagulation were characteristic of the severe allergic phenotype.

Conclusion: In this follow-up study, we found that severe patients have a clear transcriptomic signature and, in agreement with our previous results, there are transcripts involved in platelets functions and coagulation that should be considered as potential biomarkers of allergic severity as they change in relation to the degree of allergic inflammation in different allergic populations.

TP1230 | Multiallergic patient undergoing cardiac surgery. Safety of an in vitro testing strategy

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Background: Percutaneous closure of patent foramen ovale (PFO) is the standard of care for this congenital heart defect. Surgical closure is currently limited to patients suffering from allergic reaction to components of percutaneous devices, such as nickel. Moreover in multisensitized patients drugs used during the operation and the post-operative period may trigger unpredictable allergic reaction.

Method: A 48- years-old female suffering from frequent headaches presenting as hemicranias with aura and lipotimic episodes was diagnosed patent foramen ovale with severe left to right shunt during Valsalva's monoeuvre. The brain magnetic resonance showed multiple small altered signal areas, suggestive of repeated ischemic damage, in the white substance of both hemispheres. She also reported allergic diseases as asthma and atopic dermatitis and an allergic history for different drugs, nickel, latex, food allergens and inhalants. She was continually treated with inhaled steroid and antileukotriene. Prior to surgery we evaluated allergy for drugs used during the operation and the post-operative period by Basophil Activation Test. After in vitro exposure to propofol, fentanyl, succinylcholine, cisatracurium, protamine at 1:25 and 1:125 dilution, vancomycin at 1:200 and 1:500 dilution and sodic heparin at 1:500 dilution, the patient basophils were assessed through flow cytometric analysis (FLOW2-CAST test) for CD63 expression. Histamine and tryptase were also measured as markers of mast cell activation before surgery, 24 hours after and before discharge.

Results: A percentage of basophils CD63 expression < 5% and a stimulation index < 2 were obtained, suggesting a low immunogenic potential of the tested drugs and for all tested dilutions. The patient underwent latex free surgery and the patent foramen ovale was directly closed through a right thoracotomic minimally invasive approach. The post-operative course was uneventful. Histamine and tryptase values were monitored during the operation remained unchanged.

Conclusion: Preoperative *in vitro* testing of multi-sensitized patients undergoing cardiac surgery may help to prevent dangerous allergic reaction. This strategy appears to be safe e may be tailored upon the center specific protocol of patient management. In this case, if the BAT has a sensitivity of < 50%, it has not been possible for this patient to follow the guidelines, in order to be able to perform the surgery successfully.

TP1231 | Systemic mediators are associated to oral mucosa remodelling in severe respiratory allergy

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Background: In previous studies, we demonstrated that severe phenotypes of respiratory allergy undergo oral mucosa remodelling. This remodelling occurs in the absence of inflammatory infiltrate recruitment, and independently of food allergy. This suggests that oral mucosa is an immunocompetent site that may be key in the progression of respiratory to food allergic reactions and highlight the need to understand how systemic inflammatory mediators affect mucosal integrity. In this study, we aimed to characterize systemic biomarkers associated to severe respiratory allergic phenotypes.

Method: We took advantage of previously described severe respiratory phenotypes associated to olive pollen and mites. We recruited patients with severe respiratory allergy to olive pollen from Cordoba, Spain, defined by clinical history and with positive skin prick test

(SPT) to olive allergens Ole e1 and Ole e7, and patients with severe allergy to house dust mites (HDM) from Gran Canaria, Spain, who experienced anaphylaxis after ingestion of mite-contaminated flours. We measured a panel of inflammatory mediators in the serum samples of these patients by multiplex assays in comparison with a control group of non-allergic subjects and with mild allergic patients.

Results: We observed differences in the levels of inflammatory mediators, such as IL-4 and IL-13, characteristic of Th2 immune responses associated to the severe allergic phenotypes. These mediators have been described to induce IgE production and affect epithelial barrier functions.

Conclusion: These findings suggest that systemic mediators may participate in the immune mechanisms underlying oral mucosa remodelling and severe allergic progression.

TP1232 | Diseases related to serum total tryptase measurements and diagnostic value

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Background: Measurement of serum total tryptase level (ST) is used as a biomarker for mast cell mediator-related diseases. Its use in anaphylaxis (AN) and mastocytosis is established but its full range of utility is yet to determine. The aim of this study was to assess the usefulness of the ST determination.

Method: We analysed the ST measurements performed in the Pathology department of a tertiary hospital over a 5-year period (2014-2018). The reasons for the measurement were identified and then associated with the definitive diagnosis. Patients with ST ≥ 11.4 μg/L and ≥ 20 μg/L were particularly assessed as well as those with the diagnosis of AN and mastocytosis. AN was defined as per EAACI criteria and mastocytosis as per WHO criteria. Statistical analysis was performed in *SPSS 24*®.

Results: A total of 1124 ST were analysed, corresponding to 893 patients (mean age 43.4 ± 19.6 years). Only 8% had acute symptoms at tryptase investigation.

The most frequent reasons for the determination of ST were AN (30%), angioedema or urticaria (17%), hymenoptera sting reaction (16%), drug hypersensitivity reactions (DHS) (8%) and cutaneous mastocytosis (CM) (5%).

AN lead to diagnosis of systemic mastocytosis (SM) in 11 cases (4% of AN) with the hymenoptera stings being the main trigger (n = 7). CM lead to SM in 7 cases (26% of CM).

Angioedema, urticaria, DHS and others did not lead to any SM diagnosis.

BST exceed 11.4 μg/L in 72 patients (8% of total). Of those, 44% had levels ≥ 20 μg/L and SM diagnosis was confirmed in 69%.

Comparing the ST between the different diagnostics, it was significantly higher in SM than in AN, urticaria, angioedema or others ($P < 0.05$). Mean ST for SM was 65.6 ± 99.9 μg/L and mean acute ST for AN was 12.4 ± 12 μg/L.

Of the AN with acute and baseline ST (n = 27) the median rise was 241% (34% to 1309%) and of those with ST < 11.4 μg/L (n = 11) the median rise was 56% (20% to 143%).

Higher levels of acute ST (75th percentile 11.4 ng/mL) showed high specificity (80%) and PPV (0.78) for AN but showed low sensitivity (30.6%) and NPV (0.2).

Conclusion: Tryptase was predominantly measure in the diseases where it has confirmed diagnostic value: anaphylaxis and mastocytosis. Levels > 20 ng/mL are a strong indicator of SM, even though lower levels cannot exclude mastocytosis. The mean rise of acute over basal ST shows evidence of mast cell activation especially in AN. A rise of 50% increases the diagnostic value of ST. A normal acute ST does not exclude AN.

TP1233 | Allergy to live fish bait

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Case Report:

Background: Larvae of insects and worms used as live fish bait are a common cause of allergy in anglers. Asticot maggots (Blowfly, Calliphoridae family) are the most important live bait used for angling in our country.

Material and Methods: We present a 41-year-old male, fond of fishing, who developed respiratory and skin symptoms thirty minutes after exposure to asticot maggots (white and red variety) used as live bait. The purpose of this study was to determine the molecular mass of the allergens involved in this case. Immunology tests were performed to confirm the diagnosis.

Results: The study was performed by SDS-PAGE immunoblotting assay according to Laemmli under reducing conditions (with 2-mercaptoethanol): IgE-binding bands of aprox. 80 kDa; 28.5 kDa; 16.5 kDa; and 12 kDa were detected. Skin prick tests were negative to common aeroallergens and positive to aqueous extract of asticot maggots (white and red variety). Allergy to maggots used as fishing bait has been previously described as well as some IgE binding bands with molecular mass similar to those detected in our study.

Conclusions: In our case, the presence of serum specific IgE against proteins from fly larvae (white, and red) have been detected; this sensitization could justify an allergic reaction by exposure or contact with these allergenic sources.

MONDAY, 3 JUNE 2019
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ALLERGIC RHINITIS AND ATOPY IN CHILDREN

TP1235 | High prevalence of nasal allergy development in infants with atopic dermatitis and/or food allergy: A prospective cohort study

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Background: Allergic rhinitis (AR) is a major risk for asthma and several cohort studies reported that AR starts early in life. However, there have been few studies of longitudinal follow-up to clarify nature of AR development.
Method: This study was based on children who participated in the IRAM (Impact of Rhinitis on Atopic March; UMIN000004157) cohort. The study was a multi-center, prospective five visit study during 2 years. Inclusion criteria for this study were less than 2 years of age at entry, physician-diagnosed atopic dermatitis (AD) and/or food allergy (FA). Clinical symptoms of AR, nasal eosinophils, specific IgE (sIgE) to common food and inhalant allergens including house dust mite (HDM) and peripheral blood eosinophils were annually evaluated. After 2 years, further follow-up was continued at one center
Results: A total of 304 children was enrolled and 242 children completed 2-year-follow-up (Clin Mol Allergy 2017;15:4). Twenty-nine subjects were further followed up at our center for 6 years. Prevalence of persistent nasal symptoms (runny nose, sneezing and stuffy nose) was 48% at entry and increase yearly to 90% at 6 years. Geometric means for HDM-sIgE were 1.2 and 40 kUA/L at entry and 6 years, respectively. Eosinophils in nasal discharge were detected in 24% at entry and 72% at 6 years.
Conclusion: Prevalence of nasal symptoms of AR, HDM sensitization and nasal eosinophilia increased during preschool years in children who had AD/FA in infancy. AR may be very common in young atopic children.

TP1236 | The deficiency of vitamin D3 is associated with allergic rhinitis and sleep problem

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Background: Sleep deprivation among children inhibits pre-frontal lobe functions, such as working memory, judgment, and insight, resulting in impairment of learning and school performance and quality of life. It is well known that seep problem is associated with allergic rhinitis (AR), but there is no study about the association between seep problem with level of vitamin D_3 and nasal cavity volume.
Method: We distributed the ISAAC and 27-item questionnaires, including the pediatric daytime sleepiness scale (PDSS) and questions related to sleep pattern, sleep satisfaction, and emotional state, to 615 children. We also investigate other factors to sleep problem, such as sensitization to allergen, nasal cavity volume, and the level of vitamin D_3, ferritin, and hemoglobin.
Results: The 111 children had sleep problem (18.0%, male 49.5%). The level of vitamin D_3 was associated with the quality of sleep (r = −0.114, P = 0.012). After adjust gender, age, body mass index, location, parental allergic history, prematurity and/or low birth weight, increased the level of vitamin D_3 (aOR 0.939, 95% CI 0.895 to 0.985, P = 0.009) and nasal volume (aOR 0.857, 95% CI 0.761 to 0.964, P = 0.010) were associated with the quality of sleep. Children with AR were associated with the quality of sleep (aOR 1.642, 95% CI 1.023 to 2.636, P = 0.040). The level of vitamin D_3 < 20 ng/dL were associated with the quality of sleep (aOR 1.776, 95% CI 1.071 to 2.945, P = 0.026).
Conclusion: The level of vitamin D_3 was strongly associated with the quality of sleep, independent with nasal volume and AR.

TP1237 | Childhood atopic status in relation to rhinitis in adolescence and early adulthood

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Background: During past decades, there has been an alarmingly increase in prevalence of childhood rhinitis around the world including Taiwan. However, it remains largely unexplored whether childhood atopic status has impact on subsequent development and persistence of rhinitis in adolescence and adulthood. As such, in this study, we investigated the relationship of atopic status in childhood stage with rhinitis in adolescence and early adulthood in a prospective population-based Asian schoolchildren cohort, the Prediction of Allergies in Taiwanese CHildren (PATCH) study.
Method: A total of 1315 schoolchildren (median age: 10 years, interquartile range: 8-11 years) participating in the PATCH study were included in this study. Briefly, the PATCH study launched in 2007, aiming to investigate the epidemiology and predictive factors related to asthma and allergies in children. Childhood atopy was defined by Phadiatop Infant at enrollment. We used a modified International

Study of Asthma and Allergies in Childhood (ISAAC) questionnaire to collect demographic, epidemiologic, and clinical data such as clinical symptoms and diagnosis of allergic diseases including rhinitis at enrollment and the 6 year follow-up, respectively. Multiple logistic regression models with covariates adjustment were performed to investigate the association between atopic status at childhood stage and rhinitis in adolescence and early adulthood.

Results: Among the 1315 study children, 752 (57.2%) children had atopy at enrollment. Childhood atopy at enrollment was positively associated with rhinitis ever (adjusted odds ratio (AOR) = 4.03, 95% confidence interval (CI): 2.89-5.61), current rhinitis (AOR = 3.73, 95% CI: 2.68-5.20), and physician-diagnosed rhinitis (AOR = 3.72, 95% CI: 2.65-5.22), respectively, during a follow-up study in adolescence and early adulthood. In addition, among children having current rhinitis at enrollment, there was a positive association between childhood atopy and persistent symptoms of rhinitis during follow-up (AOR = 3.93; 95% CI: 2.13-7.24).

Conclusion: Our results indicate positive associations between childhood atopy and rhinitis in adolescence and early adulthood. Further investigations in relation to underlying mechanisms are needed.

TP1238 | Nasal provocation can be useful for diagnosing children with local allergic rhinitis

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Case Report:

Introduction: Local allergic rhinitis is characterized by symptoms of allergic rhinitis without a positive skin prick test or detection of specific immunoglobulin E (IgE) against aeroallergens. These patients were often misdiagnosed as having "non-allergic rhinitis" (NAR) in the past. However, there can be evidence for a specific IgE-production in the nasal mucosa in these patients without systemic sensitization.

Case Report: A 10-year-old boy admitted to our department of pediatric allergy complaining of a perennial nasal obstruction. Therapy with mometasone nasal spray had shown an intermittent improvement of the nasal obstruction. He had a history of recurring obstructive bronchitis during early childhood, since the age of 6 years he had no more asthmatic symptoms. He had no atopic dermatitis and no food allergies. There were no pets living in the house. The patient had a history of polypectomy and signs of sinusitis in cranial magnetic resonance imaging (MRI). Family history for atopic disease was positive with both parents suffering from an allergic rhinitis with proven allergies against aeroallergens. A blood test had shown an elevated IgE of 226.6 IU/mL (reference range < 120 IU/mL) and a mild sensitization against cat. There was no specific IgE against house dust mite, dog, birch, grass pollen, mugwort and mold. We performed a skin prick test for aeroallergens with a positive result for cat epithelium. Due to the suggestive symptoms we subsequently performed a nasal provocation test with house dust mite which showed an impressive positive result. Patient was suffering from nasal secretion, itching of the eyes and coughing and even the lung function test after the provocation showed a significant decrease of the forced expiratory volume in one second (FEV 1). Therefore, a local allergic rhinitis with sensitization against house dust mite could be proven and we recommended a specific subcutaneous immunotherapy.

Conclusion: In patients with symptoms of an allergic rhinitis but without evidence of a positive skin prick test or specific IgE against aeroallergens a local allergic rhinitis should be considered and a nasal provocation test should be performed.

TP1239 | Olfactory dysfunction in children with moderate to severe allergic rhinitis

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Background: Olfactory dysfunction is often experienced in patients with allergic rhinitis (AR). However, there have been only a few studies which rely on quantitative measurement of for olfactory function in children with AR.

Method: Thirty children with AR and 10 children without AR (control group) aged 6–9 years were recruited from July 2016 to November 2018. Odor identification test (sniffin' sticks; 12-item) was performed and the results were compared between AR group and control group. Sinus X-ray (Waters' view) was evaluated for AR group. In addition, intranasal mucosa findings, nasal secretion eosinophil, blood eosinophil counts, total immunoglobulin E (IgE) levels, cedar-specific IgE, and dermatophagoides pteronyssinus-specific IgE were also evaluated for all participants. Patients' guardians provided written informed consent.

Results: No significant difference was observed in sniffin' sticks score between AR and control groups [means ± with SD, 8.53 ± 2.50 vs 9.90 ± 1.66; P = 0.116]. However, the score in AR group with moderate to severe intranasal mucosa findings was significantly lower in comparison with control group [8.25 ± 2.53 vs 9.90 ± 1.66; P = 0.036].

Conclusion: Nasal mucosal findings correlated with olfactory dysfunction in children with AR. Further investigations are necessary to clarify the reactivity for AR treatment and prognosis.

TP1240 | Local atopy in childhood adenotonsillar hypertrophy

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Background: Although the cause of adenotonsillar hypertrophy remains unknown, some studies have shown that allergy may be a risk factor. This study determined the levels of allergen-specific immunoglobulin E (sIgE) in the adenotonsillar tissues of children with adenotonsillar hypertrophy and evaluated the clinical significance of local atopy in adenotonsillar tissues.

Method: We measured 21 types of specific immunoglobulin E in the serum and adenotonsillar tissues of 102 children with adenotonsillar hypertrophy and compared the sensitization patterns of the serum and local tissues. The patients were divided into three groups—atopy, local atopy, and nonatopy—according to the sensitization of serum and adenotonsillar tissues, and the clinical symptoms among the groups were analyzed.

Results: Seventy-two (70.6%) children with adenotonsillar hypertrophy were sensitized to more than one allergen in the serum and/or adenotonsillar tissue. Thirty (29.4%) children had no IgE positivity to any allergen in both serum and adenotonsillar tissues. Fifty-five (53.9%) were sensitized to at least one allergen in the serum. Seventy (68.6%) were sensitized to at least one allergen in the adenotonsillar tissue. Seventeen (36.2%) of 47 children with specific immunoglobulin E negative serum had specific immunoglobulin E-positive adenotonsillar tissues. The rate of specific immunoglobulin E was significantly higher in local tissues than in serum. The rate of inhalant allergen specific immunoglobulin E was significantly higher in the adenoids than in the tonsils. However, the rate of food allergen specific immunoglobulin E was significantly higher in the tonsils than adenoids. The lifetime prevalence of asthma and allergic rhinitis, recent symptoms or treatment of allergic rhinitis, and severity of nasal symptoms (rhinorrhea, sneezing, and nasal itching) were significantly higher in children with local atopy than with nonatopy.

Conclusion: These results confirm that allergic response may be a risk factor for adenotonsillar hypertrophy. Local allergic inflammation may play an important role in childhood adenotonsillar hypertrophy, and local atopy in adenotonsillar tissues can cause respiratory allergic symptoms in children.

TP1241 | A polycentric, randomized, double blind, parallel-group, placebo-controlled study on a nutraceutical as add-on treatment in children with allergic rhinoconjunctivitis: Phase I during active treatment

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Background: Allergic rhinoconjunctivitis(AR) treatment is usually pharmacological in children, but medications are merely symptomatic, could not be completely effective, and may have relevant side effects. Thus, doctors and parents look at complementary medicine, including nutraceuticals. A multicomponent oral nutraceutical contains extract of Perilla, quercetin, and Vitamin D. It has been reported that adults with AR diminished allergic symptoms and medication use during this oral nutraceutical therapy. Therefore, the current polycentric, randomized, double blind, parallel-group, placebo-controlled study aimed to evaluate the efficacy and safety of this oral nutraceutical as an add-on treatment in children with AR.

Method: 146 children (94 males and 52 females, mean age 9.1 ± 1.88) were randomly assigned to the oral nutraceutical+ standard treatment or Placebo + standard treatment and visited at baseline (W0), after 2 (W2) and 4 weeks (W4). Standard treatment consisted of continuous antihistaminic schedule. The primary endpoint was the Total Symptom Score (TSS - last 12 hours) change from the baseline at the end of the 4-week treatment.

Results: Both groups significantly ($P < 0.0001$ for both) reduced TSS (last 12 hours) after 4 weeks (Dchange: - 63.6% in the oral nutraceutical-group and – 60.7% in Placebo-group; P = n.s. intergroup analysis). Notably, 24 children had symptom worsening between W2 and W4: 8 in oral nutraceutical-group and 16 in Placebo-group, with significant intergroup difference ($P < 0.05$). All of them were poly-allergic subjects exposed to multiple allergens. There was no relevant adverse event.

Conclusion: The present study documented that the multicomponent oral nutraceutical containing extract of Perilla, quercetin, and Vitamin D, as add-on treatment, was able to significantly prevent the occurrence of clinical worsening and was safe in AR poly-allergic children.

*Italian Study Group on Pediatric Allergic Rhinoconjunctivitis: Cardinale F, Cherubini S, Giordano P, Leonardi S, Marchisio P, Martelli A, Minasi D, Miraglia del Giudice M, Paravati F, Pellegrini G, Podestà A, Pogliani L, Salpietro C, Tosca MA, Verrotti A, Zicari A.

TP1242 | A polycentric, randomized, parallel-group, study on a multicomponent nutraceutical, as preventive treatment in children with allergic rhinoconjunctivitis: Phase II

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Background: Allergic rhinoconjunctivitis(AR) treatment is commonly based on the use of antihistamines and intranasal corticosteroids, but the medications do not cure AR, could not be completely effective, and may have also relevant side effects. Thus, doctors and parents look at complementary medicine, including nutraceuticals. A novel oral nutraceutical contains extract of Perilla, quercetin, and Vitamin D and hence exerts anti-inflammatory, immune-modulatory, and anti-allergic activity. The current polycentric, randomized, parallel-group, controlled study aimed in the Phase II to evaluate the efficacy and safety of this oral nutraceutical in preventing AR exacerbations in children after the end of the pharmacological treatment.

Method: 128 children (94 males and 52 females, mean age 9.1 ± 1.88) completed Phase II. Sixty-four children continued oral nutraceutical treatment (Nutraceutical Group) and 64 ones did not assume any medication (Observation Group) for 4-12 weeks. The study endpoints were the duration of symptom-free or with mild symptoms, the number, intensity and duration of exacerbations.

Results: Children of Nutraceutical Group halved the risk (HR = 0.54) of having AR exacerbation and less ones experienced a significant reduced number (P = 0.039) of AR exacerbation than Observation Group. There was no relevant adverse event.

Conclusion: The present study documented that prolonged assumption of the multicomponent oral nutraceutical, containing extract of Perilla, quercetin, and Vitamin D, was safe and able to significantly reduce, such as halving, the risk of AR exacerbation after the suspension of one-month antihistamine treatment in children with allergic rhinitis.

* Italian Study Group on Pediatric Allergic Rhinoconjunctivitis: Cardinale F, Cherubini S, Giordano P, Leonardi S, Marchisio P, Martelli A, Minasi D, Miraglia del Giudice M, Paravati F, Pellegrini G, Podestà A, Pogliani L, Salpietro C, Tosca MA, Verrotti A, Zicari A.

TP1243 | Total antioxidant status (TAS), pulmonary function and nutritional status in children with allergic rhinitis. A six-month follow-up study

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Background: Compared with asthma, the role of oxidative stress in allergic rhinitis (AR) has received little attention. Aim: to evaluate total antioxidant status (TAS), pulmonary function and nutritional status in children with AR during exacerbation and plateau of allergic disease.

Method: TAS level within plasma were determined photometrically (an enzymatic reaction, kit Immunodiagnostic AG, Bensheim, Germany) in 44 (23M/21F) children with AR twice, at the exacerbations of AR (Time0 = T0) and after a six months after (Time1 = T1). Pulmonary function test (PFT) was performed by spirometer (Jaeger, Germany), and nutritional status by anthropometry assessment and bioimpedance (Bodystat1000). Type of allergens, exposition to smoke, physical activity were recorded.

Results: An increased level of TAS was observed in T0 assessments as compared to T1 (1.24 ± 0.64 vs 1.89 ± SD 0.99 μmol Trolox Eq/L; $P < 0.005$). There was no significant difference in PFT (FEV1-88.6%pv, FVC-90.35%pv, FEV1/FVC-81.9) and nutritional status (weight 66 ± 22.7, height 159 ± 17.8, FAT% 21 ± 8.9), between the T0 and T1 examination of the patients. There was correlation between TAS and weight in T0; $P < 0.05$, $r = -0.36$, but no between TAS and height, FAT, type of allergens (dust mite vs grass pollen), exposition to smoke, physical activity in both T0 and T1.

Conclusion: TAS in children with AR is within normal range and rose significantly during exacerbations of allergic disease, while pulmonary function and nutritional status does not changes. Analysis of TAS might be helpful in monitoring the clinical treatment of children suffering from AR. The value of TAS does not depend on body weight, height, fat, type of allergens, exposition to smoke, physical activity.

TP1244 | Assessment of leukotriene E4 as a marker of inflammation in allergic rhinitis children with antihistamine/leukotriene receptor antagonist and leukotriene receptor antagonist

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Background: Recent studies have shown that the cysteinyl leukotriene (cysLT) of exhaled breath condensate (EBC) could be predictive of inflammatory status and effectiveness of treatment in allergic disease. The aim of this study was to evaluate the inflammation and therapeutic effectiveness with cysLT in EBC of pediatric allergic rhinitis (AR) with different drugs.

Method: We enrolled 44 healthy children (median age, 4 years 3 months) and 47 AR children (median age, 4 years 8 month). All of AR patients received intranasal steroid (fluticasone furoate) once per day for 2 weeks. After 2 week fluticasone furoate treatment, they were classified into two groups (levocetirizine/montelukast group (LM) and montelukast group (M)) and we treated each group for another 10 weeks. To evaluate the therapeutic effectiveness, we used symptom score (SS) and EBC leukotriene E4 (LTE4). EBC samples were collected with RTube. Each parameter was checked at 0, 2, 12 week therapeutic period.

Results: Most AR patient showed clinically improvement with 2 and 12 week fluticasone therapy (0 wk SS = 7.6, 2 wk SS = 4.2, 12 wk SS = 1.8 $P < 0.01$ in LM group; 0 wk SS = 7.8, 2 wk SS = 3.8, 12 wk SS = 1.9 $P < 0.01$ in M group). There was not any statistical difference between both groups. LTE4 levels of AR were higher than healthy control (0 wk 68 vs 15 pg/mL), and were reduced after 2 week fluticasone treatment (75.2 → 31.4 pg/mL, $P < 0.01$ in LM group; 73.6 → 33.1 pg/mL, $P < 0.01$ in M group). After 12 weeks treatment, there were no different level of LTE4 in LM and M group.

Conclusion: LTE4 in EBC assessment may be useful in the evaluation of inflammation of allergic rhinitis. Levocetirizine/montelukast combo and montelukast show same therapeutic efficacy.

TP1245 | Dog ownership and farm exposure during pregnancy are associated with increased interferon-gamma production by cord blood mononuclear cells

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Background: Epidemiological and observational data suggest that farm and pets exposure in early childhood may be conducive to reduced atopy. Currently, there is a lack of consensus regarding underlying immunological mechanisms, especially in the prenatal period.

Aim: We hypothesized the influence of farm exposure and pets ownership during pregnancy on intracellular interferon(IFN)-gamma production by cord blood mononuclear cells (CBMC).

Method: Intracellular IFN-gamma expressions, as well as early activation marker CD69 (absolute cells count), were examined using flow cytometry after PHA stimulation of CBMC obtained from 93 full-term newborns. Data are shown as median (25%-75% quartiles) of absolute cells count (×106/L). Statistical analysis was performed using the Mann–Whitney U-test.

Results: We revealed that newborns from rural mothers (n = 14) have a higher amount of both nonactivated ($INFgamma^+/CD69^-$, $P = 0.02$) and activated ($INFgamma^+/CD69^+$, $P = 0.028$) CBMC producing IFN-gamma as compared with newborns from urban mothers (n = 79). Only for newborns from urban mothers, we calculated the influence of pets exposure during pregnancy on intracellular IFN-gamma production. Noteworthily, that only amount of activated ($INFgamma^+/CD69^+$) CBMC was elevated in dog (27.8; 19.6-38.3) but not in cat (17.7; 8.6-20.1) exposure groups as compared with no-pets group (14.6; 7.0-26.1), $P = 0.034$ and 0.85, respectively.

Conclusion: Thus, external and home environment factors such as farm exposure and dog but not cat ownership may act prenatal affecting the IFN-gamma producing and Th1/Th2 balance already at the moment of infant's birth. These findings can leastwise partially explain previously reported epidemiological data.

MONDAY, 3 JUNE 2019
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AIT: MECHANISMS AND ALLERGENS

TP1246 | Unbiased mass cytometry analysis method applied to high-dimensional single cell phenotyping deciphers tolerance induction in a model of allergen immunotherapy

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Background: Adjuvants are useful tools to improve allergen-specific immunotherapy (SIT) effects. Based on recent evidence showing that high doses of CpG oligodeoxynucleotides (CpG-ODN) can induce immune tolerance, we develop a successful high CpG-based SIT in a murine asthma model to Fel d 1. In order to meet the need for deep immunophenotyping in the allergy field as potent tool for high-throughput analysis facing the future of personalized medicine, here we analysed mass cytometry data with a novel and unbiased method to decipher immune-tolerance mechanisms in CpG-SIT

Method: BALB/c mice were sensitized by three i.p. injections of Fel d 1 with $Al(OH)_3$. Subsequently, mice received three courses of immunotherapy i.p. using a solution of Fel d 1 and CpG-ODN (1 mM). Finally, a nasal instillation challenge using Fel d 1 was performed. Three groups of animals were considered:(ai) allergic, without SIT; (b) allergic, SIT treated and (c) untreated control. Lungs (effector organ), mediastinal lymph nodes (MLN) and spleens (systemic immune response) were analysed by mass cytometry after the challenge. High-dimensional mass cytometry data were processed using a customized reported single-cell analysis pipeline in R (Nowicka, M. *et al.* F1000Research 2017, 6:748)

Results: In the lungs, clear improvements of allergic parameters were found after CpG-SIT, among which a 15-fold decrease of eosinophil and a 10-fold decrease of mast cell ratios, as well as a significant reduction in Th2 cells (4 times) and activated Th2 cells (20 times) abundance. Th2 cells were also reduced in the MLN. Splenic naïve B and T cells ratios were strongly increased upon SIT. Simultaneously, classical T regulatory cells (Tregs), where commuted to a specific Th2 suppressing Treg type expressing Gata3. This was paralleled by a 10-fold increase in non-activated Th2 cells

Conclusion: High-dimensional single-cell mass cytometry data from a CpG/Fel d 1 SIT experimental model was analysed by an adapted bioinformatic pipeline for unbiased in-depth characterization of the immune cell changes. The analyses of lungs and secondary immune organs showed a reduction of allergic cell response supported by a shift towards a tolerizing environment in CpG-SIT treated mice. These results will shed light to further understand the mechanism by which high CpG/allergen SIT modulates the immune system towards tolerance. The methodology developed here will help to improve high-dimensional single cell analysis in a broader context of human allergic diseases and SIT

TP1247 | Assessment of pre-clinical blocking activity of a hypoallergenic birch pollen vaccine candidate

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Background: The efficacy of the novel allergen-specific immunotherapy (AIT) candidate BM41 for the treatment of birch pollen allergy is evaluated within the EU-funded project "BM4SIT – Innovations for Allergy" (www.bm4sit.eu). BM41 was designed as a hypoallergenic variant of the major birch pollen allergen Bet v 1 with reduced IgE-reactivity but maintained T-cell recognition. In course of pre-clinical analysis, we sought to investigate the induction of specific serum IgG (IgG1, IgG2a, and IgG2b) and IgE antibodies in Wistar rats immunized with BM41, the treatment-relevant cross-reactivity of the induced BM41-specific antibodies towards Bet v 1, and the capability of the induced antibodies to act as IgG blocking antibodies.

Method: Wistar rats received bi-weekly injections of the intended human clinical dose of BM41 over a period of 6 months. Aluminum hydroxide was used as adjuvant. The placebo control animals received only the adjuvants. The study protocols and procedures were reviewed and approved by the National Animal Experiment Board of Finland (licence number ESAVI 8528/04.10.07/2015). Endpoint titer of serological BM41 and Bet v 1-specific IgE, IgG1, IgG2a and IgG2b levels were determined by ELISA. Using mediator release assays, the cross-linking capacity of the induced IgE antibodies with Bet v 1 and BM41 was examined. Inhibitory activity of rat sera was measured by IgE-FAB assay using an indicator serum of birch pollen allergic patients.

Results: BM41 was found to effectively induce Bet v 1- and BM41-specific IgG1 and IgG2a antibodies (10^5-fold and 10^3-fold higher compared to the placebo group, respectively). Concerning IgE reactivity, the induced antibody levels were low or undetectable. These results were consistent with the observed lack of release

in mediator release assays. Compared to the placebo group, IgG of BM41-immunized rats was able to significantly inhibit CD23-Mediated IgE-facilitated allergen binding.

Conclusion: In Wistar rats, BM41 induced a robust IgG immune response cross-reactive with Bet v 1. These results are promising regarding the induction of blocking IgG antibodies and pave the way for a prospective first-in-men clinical trial. In addition, the lack of an IgE response that might decrease the risk of side effects is an advantageous feature of BM41.

TP1248 | Sensitization pattern of the new HDM major allergen Der P 23 in Japanese HDM hdm allergic rhinitis patients

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Background: Recently, Der p 23 has been recognized as a new house dust mite (HDM) major allergen due to a high prevalence of sensitization in different populations. Sensitization to Der p 23 may be linked to the development of asthma in HDM allergic patients but the correlation to rhinitis symptoms has not been investigated. This study aimed to investigate the frequency of sensitization with Der p 23 in Japanese HDM allergic rhinitis (AR) patients and to examine the correlation between Der p 23 sensitization and AR symptoms.

Method: Blood samples (n = 120) were used form Japanese HDM AR patients without asthma (TO-203-3-2 trial; *Okubo et al*, JACI 2017;139:1840-8). Allergen-specific IgE at baseline was measured by ImmunoCAP (Der p extract, Der p 23) or ISAC (Der p 1, Der p 2) (Thermo-Fisher). For the immunological analyses, patients were divided into three age groups (12-17, 18-39, 40-64 years).Total combined rhinitis score (TCRS) was assessed according to the trial protocol.

Results: Japanese HDM AR patients were sensitized to Der p 1, Der p 2 or Der p 23 (94.2%, 97.5% and 67.8% respectively). There was no difference in the prevalence of Der p 1 and Der p 2 IgE between the age groups. But the prevalence of Der p 23 IgE was significantly higher in the two younger age groups compared to the 40 to 64-year group. Although a significant moderate correlation was found between the concentrations of IgE towards Der p extract and Der p 23 (r = 0.68), Der p 1 and Der p 23 (r = 0.58), Der p 2 and Der p 23 (r = 0.53). No significant correlation was found between the level of Der p 23-specific IgE and TCRS (r = 0.02). Interestingly, one patient without sensitization to Der p 1 and Der p 2 sensitized to Der p 23.

Conclusion: Japanese HDM AR patients showed a high frequency of sensitization to Der p 23, demonstrating Der p 23 as a major HDM allergen by prevalence in this population. Although degree of Der p 23 sensitization has little role in the severity of AR, Der p 23 may be the pathogenic allergen when Der p 1 or Der p 2 were not sensitized in HDM AR patients.

Further investigation is required for specially more younger age of HDM AR patients or allergic asthma patients.

TP1250 | Epicutaneous immunotherapy (EPIT®) protects from anaphylaxis in cashew nut-sensitized mouse model

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Background: The prevalence of tree nut allergy has increased worldwide and cashew has become one of the most common food allergens. Moreover, cashew allergy is frequently associated with severe anaphylactic reactions. EPIT® has been demonstrated to be an effective and safe treatment for peanut and milk allergies. The aim of this study was to evaluate the capacity of EPIT® in providing protection from cashew-induced anaphylaxis in a mouse model.

Method: BALB/c mice were sensitized by intra-gastric administration of cashew extracts (1 mg per mouse) plus cholera toxin (10 µg per mouse), and then treated with EPIT®(n = 32) or placebo (n = 8). EPIT® was conducted over 8 consecutive weeks using patches applied once a week for 48 hours and loaded with four different doses of cashew proteins (500, 250, 100 and 50 µg). Four days after the last application, mice were challenged orally with 100 mg of cashew protein. Anaphylaxis was assessed by measuring body temperature every 5 minutes for 1 hour following the challenge. mMCP-1 and mMCP-7 concentrations in plasma were also measured after the challenge. The day after the challenge, mesenteric lymph nodes (mLNs) were collected for flow cytometric assessment of regulatory T cells (Treg).

Results: The decrease in body temperature was significantly reduced with EPIT® 50 and 500 µg compared to placebo (50 µg: −2.2°C ($P \leq 0.05$); 100 µg: −4.5°C; 250 µg: −5.5°C; 500 µg: −2.6°C ($P \leq 0.05$); placebo: −8.4°C). The area under temperature curve values confirmed EPIT® protects from anaphylaxis compared to placebo (for 50, 100 and 250 µg respectively −162 ($P \leq 0.05$), −198 ($P \leq 0.05$), −213 ($P \leq 0.05$); for 500 µg: −154 ($P \leq 0.01$); placebo −350). This effect was accompanied by a significant decrease of mMCP-1 and mMCP-7 concentrations in plasma (mMCP-1: 0.18 µg/mL for 50 µg ($P \leq 0.05$); 0.15 µg/mL for 100 µg and 500 µg ($P \leq 0.05$); 0.11 µg/mL for 250 µg ($P \leq 0.01$) vs 0.32 µg/mL for placebo) (mMCP-7: 834 ng/mL for 50 µg ($P \leq 0.05$), 646 ng/mL for 100 µg ($P \leq 0.01$), 560 ng/mL for 250 µg ($P \leq 0.001$) and 529 ng/mL for 500 µg ($P \leq 0.001$) vs 1763 ng/mL for placebo). A significant increase of Treg and naive Treg populations was also observed in mLNs for mice treated with EPIT® 500 µg compared to placebo ($P \leq 0.01$).

Conclusion: EPIT® was effective in protecting sensitized mice from anaphylaxis in this cashew-allergic mouse model.

TP1251 | Expression of MicroRNAs during venom immunotherapy does not correlate with basophil activation test

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Background: MicroRNAs are small non-coding molecules regulating functioning of immune system. In allergic diseases they have an influence on eosinophils development, T cells differentiation and activation, development and activation of mast cells. Although our knowledge about role of microRNAs in several allergic diseases has considerably expanded over the last years, some areas warrant future investigation. One of them is the role of microRNA in the process of regaining of allergen tolerance during immunotherapy. The aim of the study was to determine the expression of selected microRNAs during the immunotherapy with wasp venom and investigate the relations between changing microRNA expression and reactivity of effector cells.

Method: Five adult patients with a history of severe systemic reaction after stinging by a wasp (grade III or IV in Mueller's classification) and sensitization to wasp venom confirmed by skin tests and sIgE were included. Initial phase of wasp venom immunotherapy (VIT) was performed according to ultra-rush protocol. Consecutively maintenance doses were administered every 4-5 weeks. Venous blood was collected before VIT, 24 hours after completing initial phase and after 3 months of maintenance therapy.

Control group was comprised of five healthy individuals with no history of allergy. Blood sampling was performed once.

Basophils activation test (BAT) was performed within 24 hours after sampling. Expression of 96 microRNAs was determined with the use of microfluidic cards. In statistical analysis their expression was compared between the study groups as well as between pre-VIT and post-initial phase and maintenance phase samples with the 2-fold difference as a significant.

Results: Significant differences were found between patients with wasp venom allergy and healthy controls in the expression of miR-601 and miR-1201 ($P < 0.05$). After 3 months of VIT the profile of microRNA was changed with lower expression of 6 microRNA (including miR-182, miR-342, miR-375) and higher of 11 microRNAs (including let-7d, miR-34b, miR-143). However, the changes in the expression were not associated with the results of basophil activation test.

Conclusion: VIT has led to changes in the expression of microRNA associated with Th2-type inflammation and tolerance induction. However, expression pattern did not correlate with BAT.

TP1252 | An adjuvant systems approach to develop vaccines against challenging diseases: Dioleoyl phosphatidylserine (DOPS) confers enhanced protection against malaria for VLP-TRAP based vaccines

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Background: Harnessing the power of next-generation adjuvants or adjuvant systems can provide a significant advantage in the development of prophylactic vaccines for emerging and/or challenging diseases. Virus-like particles provide a highly immunogenic scaffold for antigen presentation and can be combined with other adjuvants to form an effective adjuvant system to enhance induction of protective immune responses. In this study we assessed the potential of Dioleoyl phosphatidylserine (DOPS) to serve as an adjuvant in the development of a vaccine against malaria either alone or combined with VLP using *Plasmodium falciparum* thrombospondin-related adhesive protein (TRAP) as a target antigen.

Method: The TRAP antigen was chemically coupled to VLPs derived from the cucumber mosaic virus fused to a universal T cell epitope of tetanus toxin (CuMVtt). Mice were immunized with TRAP alone or formulated in alum or DOPS and compared to TRAP coupled to CuMVtt formulated in PBS or DOPS. Induced immune responses, in particular T cell responses, were assessed as the major protective effector cell population induced by TRAP. The protective capacity of the various formulations was assessed using a transgenic *Plasmodium berghei* expressing PfTRAP.

Results: The humoral and T cell immunogenicity of PfTRAP when formulated with adjuvants increased significantly compared to the antigen alone. The adjuvant system of DOPS formulated with display on VLP's induced the strongest and most protective immune response. DOPS was able to significantly increase the IgG2a responses but also Th1 and CD8 + T cell responses.

Conclusion: The combination of VLP with DOPS as an adjuvant system optimally enhanced induction of protective immune responses, and may be an attractive adjuvant combination useful for the development of novel prophylactic vaccines in areas of challenging or emerging diseases, particularly where optimal Th1 responses is sought.

TP1253 | In vivo and in vitro efficacy of a modified aluminum hydroxide-adsorbed extract of house dust mite subcutaneous immunotherapy in sicilian allergic patients

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Background: Modified aluminum hydroxide-adsorbed extract of HDM (PURETHAL®, Hal Allergy BV, Leiden, The Netherlands) for subcutaneous use is prescribed in moderate-severe allergic respiratory diseases patients inadequately controlled despite the use of medication. It has been demonstrated that SIT positively affects clinical and immunological parameters. However, its effect on basophil activation remains unclear. We investigated the effect of SIT on basophils and concomitantly assessed its clinical efficacy in HDM sensitized patients.

Method: In a single-center, 29 HDM allergic patients (M/F = 20/9; mean age 28.55 SD ± 15.70 years) with perennial rhinitis/rhinoconjunctivitis with/without concomitant asthma, received HDM SIT (PURETHAL®). During one year treatment, evaluation of the total symptom score (TSS) and medication score was done at baseline and after 1 year. The tolerability was analysed with regard to local and systemic reactions within 30 min after the injection. 7 HDM allergic patients underwent basophil activation test before and after 12 months treatment.

Results: After 1 year treatment, a significant reduction ($P < 0.04$) in TSS and medication score was recorded. Non significant local or systemic reactions were recorded within 30 min after the injection. In comparison to baseline evaluation, the percentage of basophils expressing CD 63 were significantly decrease ($P < 0.04$).

Conclusion: HDM SIT (PURETHAL®) decreases HDM-specific basophil activation over 12 months, an effect observed in vitro and in vivo.

TP1254 | Biodegradable transdermal microneedle immunotherapy can ameliorate airway inflammation in murine asthma model

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Background: House dust mite (HDM) is a well-known cause of allergic asthma. Allergen specific immunotherapy (AIT) can modify the natural course of the disease. Conventional routes of HDM AIT used in the clinics are subcutaneous or sublingual. Limitation of subcutaneous AIT is risk of anaphylaxis, and sublingual AIT is low compliance and oro-pharyngeal discomfort. To overcome the weak points of conventional AIT, we developed a HDM loaded biodegradable transdermal microneedle immunotherapy (MNIT). We aim to demonstrate the efficacy of MNIT in murine asthma model triggered by HDM.

Method: To make HDM asthma mouse model, 5-week-old BALB/c female mice were sensitized and challenged by intranasal administration of HDM. The mice were divided into 5 groups: sham, asthma, low (10 μg) and high dose (100 μg) subcutaneous AIT, and MNIT (10 μg). To make HDM loaded MNIT patches, droplet-born air blowing method was used. Airway hyperresponsiveness, allergic inflammation markers were analyzed by broncho alveolar lavage fluid, immunohistochemistry, serum immunoglobulin (Ig) analysis, and lung cytokine assays.

Results: Airway hyperresponsiveness was ameliorated by MNIT. Eosinophilic inflammation in broncho alveolar lavage was improved without local or systemic adverse reactions. Reduction of Th2 (IL-4, IL-5, and IL-13) cytokines, and HDM specific IgE, induction of Treg (IL-10, TGF-β), Th1 (IFN-γ) cytokines was observed. Eosinophilic infiltration, goblet cell hyperplasia, and subepithelial fibrosis were also alleviated by MNIT. These changes were more significant in the MNIT group than in subcutaneous AIT group.

Conclusion: HDM loaded biodegradable transdermal MNIT is a novel treatment option to treat asthma.

TP1255 | Detection of Mollicute species (Mycoplasma) in House Dust Mites

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Background: House dust mites are living creatures used as a source material for extracts to produce immunotherapy vaccines, and in vivo diagnostics for humans. For this reason contamination of mite cultures and extracts thereof should be carefully controlled. It has been reported that bacteria and fungi are present in mites. One specific community of bacteria that could be present in mites is Mycoplasma. There are four types of Mycoplasma species known to be pathogenic to humans, i.e. M. pneumoniae, M. hominis, M. genitalium and Ureaplasma species. When mite extract are made, whole culture and purified mite bodies of the different mite species are used and these could therefore potentially also contain Mycoplasma species as extracts are commonly filtered using 0.22 μm filters and the average size of mycoplasma is 0.1 μm.

Method: We analyzed *Dermatophagoides pteronyssinus* and *D. farinae* mite cultures and extracts from 5 different suppliers for the presence of mycoplasmas using a PCR-based method. A total of 11 species-specific primers suitable for the detection of 11 mollicutes, as well as a universal generic-specific primer that is capable

of detecting all mycoplasma species were used. The chosen specific primers are based on pathogenic and most commonly described human mycoplasma species. As an additional confirmatory method we grew samples of mites on mycoplasma specific agar.

Results: We found that general mycoplasma presence could be detected by PCR in mite products of 5 suppliers). M. pneumoniae was detected in mite products from 4 suppliers (x, y, a, b). Live mycoplasma was shown to be present in the products of 2 suppliers.

Conclusion: This is the first report showing live mycoplasma in living mites and extracts of mites. All mite products to be used in humans should therefore be tested for Mycoplasma species and the risks of these must be assessed.

TP1256 | Analysis of the effect of vaccination against pneumococcal infection on the course of comorbid pathology in patients with chronic obstructive pulmonary disease and chronic heart failure

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Background: Congestive heart failure is the outcome of most cardiac pathologies. It is caused by COPD in 13% of cases. The most frequent etiological component of infectious exacerbations of COPD is S. Pneumonia.

Objective: To evaluate the effectiveness of vaccine prophylaxis of 13-valent conjugated pneumococcal vaccine (PCV13) in patients with COPD and CHF.

Method: 429 male patients with diagnoses of COPD, CHD and CHF were included in the study. Average age of the patients was 61.64 (95% CI; 57.34-67.19) years. The main endpoints of the 5-year-observation for evaluation of the effectiveness were: dyspnea dynamics according to mMRC, FEV1, left ventricular ejection fraction (EF), 6-MT dynamics, changes in CHF class, number of exacerbations, hospitalizations, number of pneumonia. 13-valent conjugated pneumococcal vaccine was used for vaccine prophylaxis.

Results: The severity of dyspnea in patients with combined COPD and CHF decreased from 3.12 (95% CI; 2.40-3.84) to 1.73 (95% CI; 1.39-2.57) after applying PCV13. Dynamics of FEV1: 45.93% (95% CI; 40.51-51.36) initially and 49.16% (95% CI; 44.01-54.51) after 5 years of vaccination. The dynamics of the EF: 39.15% (95% CI; 31.12-47.18) initially and 48.31% (95% CI; 41.19-55.42) after a 5-year-observation period. The number of COPD exacerbations decreased 5.3 times - from 198 to 37 cases and the number of hospitalizations 5.2 times - from 201 to 38 episodes. The cases of pneumonia decreased 7.6 times - from 38 to 5 (in 5 years). The use of PCV13 in patients with comorbidity has led to a reduction in the functional class of CHF from IV to III and II in 52% of cases.

Conclusion: An increase in the functional class of heart failure occurs with the increase in clinical symptoms of respiratory system lesions. The inclusion of PCV13 vaccine prevention in management plan of patients with combined pathology allows stabilizing the main clinical and functional indicators of the respiratory and cardiovascular systems not only in the short term but also during at least 5 years of observation. Vaccination leads to a decrease in the cases of pneumonia, the number of exacerbations of COPD and related hospitalizations.

TP1257 | Development of a total antigenicity IgG ELISA for the quality control of a mixed grass allergoid drug product

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Background: The European regulatory framework requires the use of validated analytical methods for characterisation and standardization of allergen products to ensure reliable quality attributes for their manufacture and control. Grass MATA MPL is an adjuvanted mixed-grass allergoid adsorbed to Microcrystalline Tyrosine and Monophosphoryl Lipid A adjuvants. Development and validation of a total antigenicity (IgG) potency assay for Grass MATA MPL has been developed using polyclonal rabbit IgG-antibodies, using the modified allergen product as the immunogen.

Method: Rabbits were immunized with a mixed grass modified extract of *Poaceae* species. Specificity of the serum was determined using ELISA and Western blotting. A total IgG ELISA potency assay for quality control of complex grass allergoids was developed and validated based on IgG epitope specificity in line with ICH Q2(R1) guidelines.

Results: Grass-specific polyclonal rabbit IgG-antibodies raised against a mixed grass modified allergen product exhibited high specificity for IgG-binding epitopes using direct ELISA dose-response assessments. Validation parameters including specificity, linearity, accuracy and precision were established in accordance with ICH Q2(R1) guidelines.

Conclusion: An IgG-based ELISA for Grass MATA MPL provides an essential test for the determination and monitoring of allergoid potency during manufacture and drug product stability.

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ASTHMA CLASSIFICATION, SCORING AND TREATMENT IN CHILDREN

TP1258 | Prevalence of asthma, respiratory symptoms and allergic diseases in children aged 13-14 in Katowice (Poland) – results of a cross sectional study

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Background: The prevalence of childhood asthma and allergic diseases change over time and up to date information within regions are required to understand public health impact and potential gaps in care.

Method: The study was carried out as part of the Global Asthma Network - an international, multicentre cross-sectional study. Questionnaires, via schools, were addressed to all children aged 13-14 yrs living in Katowice, Poland. Children self-completed the questionnaires during class time. The questionnaire was modelled after the ISAAC questionnaire.

Results: Data were obtained from 1314 (response rate: 82.1%) children. Of these, 45.9% were boys (B) and 54.1% girls (G). The mean age was 13.6 ± 0.5 years.

Self-reported asthma prevalence was 8.8% (B: 9.7%, G: 7.7%, $P = 0.2$) while prevalence of asthma diagnosed by physician was 7.5% (B: 8.7%, G: 6.2%; $P = 0.1$). In children with an asthma diagnosis, 59.6% (B: 55.8%, G: 61.4%, $P = 0.4$) were currently treated by inhaled drugs and 40.4% using oral drugs 40.4% (B: 32.7%, G: 50%, $P < 0.05$). Chest wheeze ever was present in 18.4% of children (B: 13.9%, G: 22.3%, $P < 0.05$). Wheeze during last 12 months was present in 10.5% of children (B: 7.2%, G: 13.2%; $P < 0.05$). Among those with wheeze in the past 12 months, frequency was reported as 1-3 attacks in 75%, 4-12 in 14%, over 12 in 11%. Among the children, 16.7% (B: 11.5%, G: 21.1%, $P < 0.05$) reported wheeze during or immediately after sports. Allergic rhinitis prevalence was 27.8% (B: 25.5%, G: 29.6%, $P = 0.2$), with 17.7% reported confirmed by a physician (B: 18.7%, G: 16.9%, $P = 0.4$). Atopic eczema ever was present in 7.2% of children (B: 3.7%, G: 9.9%; $P < 0.05$), with 4.1% confirmed by a physician (B: 1.7%, G: 6.1%, $P < 0.05$). At least one allergic disease was present in 57.4% of children with asthma.

Conclusion: Allergic diseases affect almost one third of the teenage population. The prevalence of asthma was higher in boys compared to girls, but respiratory symptoms as well as the other allergic diseases were more frequent among girls.

TP1259 | L-ficolin plasma concentration and FCN2 gene Rs17549193 And Rs7851696 polymorphisms in asthmatics children

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Background: The lectin-mediated activation of complement is one of the important pathways of the first line non-specific defense against infections. Currently, only a few molecules are known to activate the lectin pathway of complement activation: collectins such as mannose-binding lectin and the ficolins. It has been shown that L-ficolin plasma concentrations were lower in children with asthma and/or allergic rhinitis (M. Cedzynski et al., 2009). The connection between asthma and L-ficolin gene (*FCN2*) polymorphisms in children populations is nor studied well, especially regarding asthma severity.

Method: 89 Caucasian asthmatic children aged 7-18 referred to a pediatric allergy center (Krasnoyarsk, Siberia, Russia) and 88 age- and sex-matched none-asthmatics (essentially healthy children without signs of infection or allergies) were included in this study. MBL levels were measured using a Ficolin-2 ELISA kit (Hycult Biotech, The Netherlands). DNA was extracted using DIAtomTM DNA Prep kits (Centre for Molecular Genetics, Russia). Genotyping was carried out using the polymerase chain reaction approach. Quantitative data are shown as median (25-75% quartiles). Chi-square and Kruskal-Wallis tests were used.

Results: We have found that in children with virus-induced asthma exacerbation (n = 78) L-ficolin plasma concentration progressive decrease with asthma severity level (Table 1). No statistically significant association were found in *rs17549193* and *rs7851696* genotypes prevalence according to asthma severity: *rs17549193*-T allele prevalence: non-asthmatics – 0.268, mild persistent asthma – 0.279, moderate asthma – 0.258, severe asthma – 0.357 ($P > 0.05$); *rs7851696*-T allele prevalence: non-asthmatics – 0.072, mild persistent asthma – 0.132, moderate asthma – 0.136, severe asthma – 0.095 ($P > 0.05$).

Conclusion: Our data suggest that relative L-ficolin deficiency may be associated with asthma severity in children. We suppose that L-ficolin insufficiency enhances susceptibility to childhood respiratory infections and may alter virus/bacteria clearance and contributes to a higher level of inflammation in the respiratory tract. L-ficolin deficiency in asthmatics children most likely have genetic nature but not associated with *FCN2* gene *rs17549193* and *rs7851696* polymorphisms.

	Persistent asthma			
Non-asthmatics (0)	Mild (1)	Moderate (2)	Severe (3)	*P*
2.26 (1.57-3.26)	8.10 (2.87-21.0)	4.99 (1.94-12.47)	4.24 (1.4-7.5)	p0-1,2,3 < 0.01 p1-3 = 0.066 Kruskal–Wallis test = 0.001

TP1260 | Asthma control assessment in children: Consistency of gina criteria asthma control test and asthma control questionnaire

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Background: To achieve full control of asthma symptoms, it is necessary to monitor its course. Until recently, the evaluation of asthma control included only the clinical parameters from the GINA (ang. Global Initiative for Asthma) criteria. Nowadays, fast methods using standardized tools are also increasingly being used for this purpose. However, none of these methods is explicitly recommended by experts.

The aim of the study was to assess the consistency in determining the degree of asthma control in children according to the ACT (ang. Asthma Control Test) and the ACQ (ang. Asthma Control Questionnaire) criteria in relation to the GINA classification.

Method: The level of asthma control in children aged 6-16 years was assessed three times within 9 months. Patients filled in the ACT and ACQ before the physician visit. In the case of ACT, the questionnaire was also completed by parents. Asthma control level was also assessed according to GINA criteria by an allergologist, who did not know the results of both tests. The analyzes were conducted in two age groups: 6-11 years and > 11 years of age.

Results: The study involved 100 children with chronic asthma with an average age of 9.53 ± 2.6 years, 77% of whom were boys. In the group of 6-11 years of age. at each visit, a statistically significant (slight and moderate) correlation was found between the degree of asthma control according to GINA and the ACQ questionnaire result (Kendall Tau-b = 0.21-0.32, $P < 0.05$). In the group of older children this tendency was observed on the first and second visit (Kendall Tau-c = 0.4, $P < 0.05$). In the case of the ACT questionnaire in both groups, a slight correlation of statistically significant importance was visible only at the second visit (Kendall Tau-c = 0.41, Kendall Tau-b = 0.39, $P < 0.05$).The statistically significant relationship was noted mainly in the case of issues related to limitation of activity and nocturnal (night-time) symptoms (*P* U Mann Whitney < 0.05).

Conclusion: On the basis of this study we can conclude that the ACQ correlate quite well with GINA criteria in predicting the level of asthma control, especially in younger children. In the case of the ACT, the results are ambiguous.

TP1261 | Assessment of the control of asthma and allergic rhinitis in children at a level II hospital

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Background: Asthma and allergic rhinitis are respiratory chronic inflammatory diseases that often coexist in children and, according to Allergic Rhinitis and its Impact on Asthma (ARIA) recommendations, control of these pathologies should be evaluated together. Therefore, Control of Allergic Rhinitis and Asthma Test (CARATKids) was developed, as the first standardized and approved questionnaire for asthma and allergic rhinitis in children aged 6 to 12 years old. The aim of this study was to evaluate the control of asthma and allergic rhinitis in children from 6 to 12 years of age, from their parents' perspective and themselves, at the pediatric outpatient of a level II hospital.

Method: Cross-sectional descriptive, observational study performed through the application of the CARATKids questionnaire between november and december of 2018. Data analysis was performed using Microsoft Excel.

Results: The study included 71 children (61% male) and their parents. The mean age was 9 years old. The most frequently complaints reported by patients in the two weeks prior to the questionnaire were sneezing (reported by 48% of patients) and cough (referred by 46% of patients). 31% of children reported asthma-related complaints during physical exercise or laughter, and 14% of children reported fatigue/difficulty performing daily life activities due to complaints of asthma or allergic rhinitis. Concerning children's parents, a minority reported morning symptoms, impact of illness on children's sleep and school absence (21%, 11% and 4%, respectively). In this study, 17% of the children had exacerbated their pathologies two weeks prior to the application of the CARAT kids questionnaire and 3% had to seek health services for medical evaluation. Most children have well-controlled asthma and allergic rhinitis (68%).

Conclusion: The systematic application of the CARATKids questionnaire allows the clinician to assess the control of asthma and allergic rhinitis, determine whether the therapy implemented is adequate or requires adjustment.

TP1262 | Allergic and non-allergic asthma across an urban-rural gradient

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Background: Asthma is a heterogeneous disease. Childhood asthma prevalence has also been shown to vary between urban and rural locations. The study of asthma phenotypes can help us understand the etiology and management of asthma as well as help explain differences between regions. We sought to compare allergic and non-allergic asthma in children between urban and rural locations as well as to identify risk factors for childhood asthma.

Method: In 2013 we completed a cross-sectional survey of urban and rural dwelling children (5-14 years, n = 3509) from Saskatchewan, Canada. Surveys were distributed through randomly selected schools for parental self-completion. Asthma was based on report of a previous doctor's diagnosis. Allergy was based on a report of a respiratory allergy, hayfever, or eczema. Multiple multinomial logistic regression (outcome categories: no asthma, non-allergic asthma, allergic asthma) was conducted to adjust for confounding.

Results: The participants were 50.2% female with a mean age of 9.3 years (SD: 2.5 years). The majority of the population lived in an urban areas (68.7%) followed by a small urban (18.5%) and rural area (12.8%). Asthma was reported by 19.1% of the population of which 69% also reported the presence of an allergic disease resulting in a prevalence of non-allergic asthma of 5.8% and the prevalence of allergic asthma of 13.2%. Rural children were less likely to have non-allergic asthma than urban children [odds ratio (OR) = 0.48, 95% confidence interval (CI) = 0.25-0.92, $P = 0.027$] but were not statistically different from urban children for allergic asthma (OR = 0.79, 95% CI = 0.54-1.17, $P = 0.247$). Having a maternal history of asthma increased the risk of non-allergic asthma ($P < 0.05$) while breastfeeding reduced the risk of non-allergic asthma ($P < 0.05$). Older age, being male, a maternal or paternal history of asthma, paracetamol use, day-care attendance, traditional medicine use, and being a firstborn child all increased the risk of allergic asthma ($P < 0.05$). Those with allergic asthma were most likely to report asthma-like symptoms such as wheeze, cough, phlegm, and shortness of breath.

Conclusion: While there was a decreased risk of asthma associated with living in a rural area, this was only seen for non-allergic asthma. Investigation of why this is occurring will help explain geographic differences in asthma prevalence and aid in the understanding of asthma mechanisms.

TP1263 | Clinical features of the bronchial asthma onset in children

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Background: Pediatric asthma in the most common chronic disease in children, with complicated differential diagnosis.

Method: 247 children in Vinnytsia region, Ukraine, with the known diagnosis of asthma were involved in the study during the period of 2016-2018 years. Children were included in the study with the asthma diagnosed for 12 months at the age of 4-11 years. 100 healthy age-matched children with no allergic disorders and known allergies in the family history comprised the control group. Obtained data were proceeded using license packs of original computer programs «STATISTICA 10.0».

Results: Asthma was diagnosed in 19 children (7.7%) at the age of 1-3 years; 72 (29.14%) at the age of 3-6 years; 156 (63.16%) at the age of 6-11 years. 136 (55.06%) of patients have relatives with allergic disorders. Child experienced 5 ± 2 wheezing episodes before the diagnosis of asthma was made. 2.0 ± 1.5 years passed from the first wheezing episode to the diagnosis of asthma Many patients (131; 53.01%) had historic diagnosis of pneumonia. Only 23 (15.56%) were proved by chest X-ray. Patients with bronchial asthma received antibiotic in 1.7 times more often than the patients of the control group during the first year of life. Low birthweight was observed in 2 (0.81%) patients with asthma and 3 (3%) in the control group. We did not observed differences in the duration of breastfeeding, time of the complementary feeding introduction and vitamin D intake at the first year of life between the main and control groups.

Conclusion: Dynamic observation is necessary for the timely diagnosis of asthma in children with virus-induced wheezing. Asthma episodes in children of the 5 first years of life are often misdiagnosed as pneumonia. We did not recognize the duration of breastfeeding and time of the complementary feeding introduction as the risk factors of the bronchial asthma development in children in our region.

TP1264 | Asthma symptom control – patient's versus physician's perspective

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Background: The main goal in asthma management is to achieve a good control of symptoms. Childhood Asthma Control Test

(c-ACT) is a validated questionnaire for parents and children, to assess asthma symptom control in children between 4 to 11 years. Our goal was to evaluate families' control perception of their children's asthma.

Method: The study was performed during the second half of 2018. The c-ACT questionnaire was applied to asthmatic patients, between 4 to 11 years, followed in a general pediatric consultation. Demographic data were analysed. Based in c-ACT results and medical evaluation symptom control using GINA criteria, patients' asthma was classified as "well controlled asthma", "partly controlled asthma" and "uncontrolled asthma". Patients' c-ACT score results were compared with medical evaluation using Chi-square independence test ($\chi 2$) to see if there was a significant different proportion.

Results: We included 69 children (average age 7.97 ± 2.17 years, 63.8% boys). The classification of asthma control according to c-ACT score and the medical evaluation results is presented in the table below. We observed that patients' asthma was classified in a significant different way by parents and doctors (*P*-value < 0.01). C-ACT and medical results were coincident in 53.6% of the answers. In the other cases, parents undervalued their children's symptoms.

Conclusion: Our data suggests that some parents do not perceive the disease symptomatology correctly. We emphasize the importance of elucidate and clarify families about the disease, its total control and the treatment goals.

	c-ACT	GINA criteria	Overlapping answers
Controlled asthma	53	23	23
Partly controlled asthma	14	37	12
Poorly controlled asthma	2	9	2
Total	69	69	37

TP1265 | Role of vocal cord dysfunction in pediatric uncontrolled asthma

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Background: Vocal cords dysfunction is a pathologic condition that can mimic or worsen asthma symptoms in children, especially elderly, and require careful differential diagnosis.

Method: We observed 127 patients at the age from 12 to 16 years (14.6 ± 1.7) hospitalized in the allergic department of Vinnytsia Regional Children Hospital during the period from 2012 to 2017 due to the lack of treatment efficacy. 69 (54.3%) of the patients were boys and 58 (45. 7%) girls, who had signs of uncontrolled asthma.

Results: There was a mismatch between the severity of asthma and effect of background therapy. 43 patients (33.8%), including 14 (32.56%) boys and 29 (67.44%) girls, had vocal cord dysfunction diagnosed through the dynamic clinical observation and repeated spirometry. Fibro-laryngoscopy is the gold standard for the vocal cord dysfunction diagnosis. It allows visualizing of discordant reduction of the vocal cord during respiration. As this method is invasive and technical complexity of its use, taking into account presence of somatoform autonomic disorders, which can be present in this group of patients, we performed spirometry. Flow-volume loop in this case has a specific appearance, that helps in diagnosing vocal cord dysfunction.

Conclusion: Vocal cord dysfunction is a common disorder in children with asthma, mimicking many cases of uncontrolled asthma. This condition should be excluded in children with uncontrolled asthma. Psychogenic cough is a frequent manifestation of vocal cord dysfunction.

TP1266 | Follow-up of patients with bronchial asthma after discontinuation of omalizumab

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Background: The efficacy of Omalizumab treatment in children with severe uncontrolled persistent asthma has been proven. However, there is a lack of data of the follow-up of children and adolescents after discontinuation of long-term omab treatment. *Objective*: to analyze and assess clinical outcomes, delayed effects and persistent response of omab therapy in children and adolescents with uncontrolled severe persistent asthma who stopped treatment.

Method: The local registry of children with uncontrolled severe persistent asthma contains data on 110 children (real-life data) receiving/stopped omab; 64 patients from previously included in the registry have reached the age of > 18 years. Among these patients, a survey was conducted (11/2018) and responses were received from 11; 6 of them - stopped omalizumab therapy. 1 (male) death was recorded as a result of severe asthma exacerbation. 1 (female) was in severe exacerbation in the absence of baseline therapy at the time of the survey.

Results: 4 of 6 patients - male. The average age - 22.5 years (27; 19), the period after the discontinuation of omalizumab averaged 4.9 (1.5; 9) years. Previously, the average of received therapy with omab in addition to basic therapy (ICS + LABA) were 3.4 (5.6; 0.9) years. The long-term therapy with omab allowed to achieve good or partly

disease control, which was persistent after the omab discontinuation: ACT-test on the background of therapy - 21.6 (20; 24) points, ACT-test after the discontinuation of omab - 21.5 (20; 23).After discontinuation of omab therapy 3 patient canceled basic therapy, of which one rarely has exacerbations and he is forced to miss work due to exacerbation of asthma. Another 3 patient continue to receive basic therapy with ICS/LABA, maintaining the same dose volume: average 500 mcg/d of fluticasone (ICS/LABA). One patient has exacerbations of food allergy, manifested by urticaria.

Conclusion: The response of omab therapy may persist after the withdrawal. Further researches are needed to clarify the optimal course of omab therapy and achieving an optimal long-term response of therapy.

TP1268 | Unexpected death in 10-yo boy with uncontrolled asthma and mega obesity – case report

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Case report:

Background: Currently, the literature rarely describe the death due to undiagnosed asthma in children. *Aim*: we described fatal asthma in child with mega obesity

Methods: The boy suffered from recurrent bronchitis every 3 month from second year of life. The 6 months ago he was admitted to the hospital due to the diagnosis of obesity. He started to be obese from 3 years of age, and now his height was 148 cm, weight −84 kg, BMI > 97centyl. He had a dyspnea during the rest and after the passage of some meters. Pulmonary function test showed mild obstruction. The polygraph examination confirmed the diagnosis of obstructive sleep apnea, AHI 47.8 (supine 31.0). The average SaO_2 value was 86%, lower than 70%. Continuous positive airway pressure was used. Good tolerance of treatment and AHI < 5 decrease (mean pressure 9 cm H_2O) were obtained. When he once again suffered from bronchitis with cough and dyspnoea, mother did not report the child to the hospital. This boy died suddenly at home the age of 10 years.

Conclusion: Asthma in obese children can be undiagnosed due to shortness of breath caused by obesity and low physical activity, and could be fatal.

TP1269 | Change of quality of life by strengthening the daily life education and instruction of medicine and inhalation about asthmatic children

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Background: I have been presented the characteristics and especially clinical future of respiratory function about asthmatic children at the congress of EAACI from 2014 to 2018 annually. This time, I studied about the strengthening the daily life education and instruction of medicine and inhalation lead to change long-term control and quality of life (QOL) about asthmatic children and family.

Method: Bronchial asthma of 54 cases (34 males, 20 females) was studied. These ages of 14 cases were less than 4 years old, and 40 cases were more than 4 years old.

Method:: 1) Materials for daily life management and guidance of taking medicine and inhalation were made.

2) A QOL questionnaire was checked before starting the study. QOL questionnaire has 11 questions, domain of physical has 3, family's emotion has 3, emotion has 2, and social has 3. Maximum point of each question was 5.

3) Condition of life and symptoms of asthma were checked by diary, asthma control test (ACT), and PEF every 2 weeks.

4) Items that were not sufficiently achieved were re-instructed at each visit.

5) QOL questionnaires were checked in 4 weeks and 8 weeks later.

6) Compared the change of QOL before and after of this study.

Results: 1) Appearance of asthma symptoms decreased after guidance.

2) Change of domain point in less than 4 years cases, physical questions before study→after 4 weeks→after 8 weeks was 4.2→4.5→4.6, family's emotion was 4.2→4.4→4.7, and emotion was 3.8→4.4→4.5. Change of domain point in more than 4 years cases, physical questions before study→after 4 weeks→after 8 weeks was 4.5→4.4→4.7, family's emotion was 4.0→4.4→4.5, emotion was 4.4→4.4→4.5, and social was 4.6→4.8→4.8.

Conclusion: Strengthening the daily life education and instruction of medicine and inhalation lead to improvement of asthma control and QOL about asthmatic children and family.

MONDAY, 3 JUNE 2019
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ANAPHYLAXIS AND NSAID HYPERSENSITIVITY

TP1270 | Anaphylaxis due to a topic application of an insect repellent solution with detected hypersensitivity to N,N-Diethyl-3-methylbenzamide (DEET)

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Background: N,N-Diethyl-3-methylbenzamide, otherwise known as diethyltoluamide or DEET, is the most common active ingredient of topical insect repellents. Apart from irritant reactions, hypersensitivity reactions described with DEET are extremely rare, ranged from contact dermatitis to urticaria and a single case of anaphylaxis has been published.

Method: A 28-year-old woman, with a history of allergic rhinoconjunctivitis and asthma by pollens, who developed tingling of lips after airborne contact of a insect repellent solution sprayed by her friend. Some minutes later she applied the same repellent on her legs experiencing oedema in lips, dyspnea, dysphagia, generalized rash and dizziness. She was treated in Emergency Department with antihistamines, several doses of adrenaline and corticosteroids being admitted in Intensive Medical Department until improvement.

No cofactors were observed in that episode.

Results: Subsequently a detailed anamnesis made suspect to the cause-effect relationship with the topic application of insect repellent in her legs. An open patch testing was conducted using the involved repellent solution. A small drop of the product was applied in the forearm of the patient, developing immediately erythema and papula of 6 × 3 centimeters in the application area, indicating a positive response. Subsequently Basophil Activation Test with the repellent solution was realized, being positive for N,N-diethyl-3—methylbenzamide (DEET).

Conclusion: We present a case of anaphylaxis after a topic application of DEET contained in an insect repellent. *In vivo* (open patch test) and *in vitro* (BAT) suggest an immediate hypersensitivity reaction IgE-mediated. We consider that possibly the inhalation of DEET has been the gateway of the sensitization of the substance, which absorption has been immeasurably enhanced by its cutaneous application. As far we know this is the second case of anaphylaxis reported in the published literature and the first one demonstrated by a BAT positive response.

TP1271 | Association between severity of anaphylaxis and coexistence of respiratory diseases: A systematic review and meta-analysis of observational studies

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Background: Respiratory diseases are associated with increased severity of anaphylaxis. Its sensitivity for predicting severity is high, although its specificity is low, owing to the marked presence of asthma in patients with food anaphylaxis in all grades of severity. We carried out a systematic review and meta-analysis to assess the influence of respiratory diseases on the severity of anaphylaxis.

Method: We searched PubMed/MEDLINE, EMBASE and the Web of Science for observational studies. The target studies were those that compared the severity of anaphylaxis between patients who had or did not have respiratory diseases. There were no restrictions based on age or sex. The studies included all the major causes of anaphylaxis (i.e. food, drugs..) or a specific cause of anaphylaxis (i.e. insect venom, radiographic contrast media).

Results: A total of thirteen studies assessed the severity of anaphylaxis in respiratory disease. These studies brought together 67 948 episodes. Respiratory disease increased the severity of anaphylaxis (OR 1.87; 95% CI, 1.30-2.70). The majority of studies were for asthmatic patients. Furthermore, the meta-analysis of adjusted and non-adjusted studies showed that asthma was associated with greater severity of anaphylaxis. The meta-analysis of adjusted studies showed heterogeneity, whereas non-adjusted studies did not. On the other hand, only one study assessed the influence of asthma on severity of anaphylaxis, without differences between mild asthma and the rest of severities.

As for the quality of evidence for the relationship between severity of anaphylaxis and respiratory disease, application of the GRADE system showed the quality of evidence to be low for asthma (with no difference between adjusted and non-adjusted studies), and very low for all respiratory diseases using individual adjusted studies and all studies.

Conclusion: Evidence showing that respiratory disease increases the severity of anaphylaxis is very low to low, although studies do not usually assess the importance of severity of asthma.

TP1272 | The diagnostic challenge of anaphylaxis in pediatric age

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Case Report: 15-year-old teenager with mild persistent asthma and mild persistent rhinitis controlled with inhaled budesonide and nasal fluticasone daily. At the first appointment in our department, he referred five previous episodes of anaphylaxis. The first episode occurred in 2012 and was described in the emergency report as "facial and lips angioedema associated with general malaise". Adrenaline was administered and he was referred to the Pediatric department for investigation. Second episode in 2013 with urticaria, angioedema, odynophagia and laryngeal tightening again treated with adrenaline; an adrenalin auto-injector was then prescribed. He presented 3 more episodes and the adrenalin auto-injector was used before ED admission. At the first Immunoallergology visit, he referred that most episodes occurred 1 to 2 hours after meals and the previous study was directed to identify a possible food allergy. A detailed diary of events was requested if new episodes of anaphylaxis or angioedema occurred. In the second visit, he had 2 new episodes of anaphylaxis, by the analysis of the diary we suspected that ibuprofen was the precipitating factor. This drug and paracetamol were frequently administered for recurrent headaches and were taken preferably during meals in order to avoid gastro-intestinal side effects. Paracetamol however had a proved good tolerance. Complete avoidance of NSAIDs was advised and a drug provocation test was planed. In 2016, despite this indication, he had a new episode of anaphylaxis after administration of ketorolac in the ED for an orthopedic pain. A provocation test with nimesulide was performed in the hospital and was negative for 100 mg. This drug is currently used as well as paracetamol when needed. He was also referred for a pediatric neurology evaluation for suspected migraine. An action plan with written instructions was given and avoidance of all other NSAIDs was advised, there were no further episodes of anaphylaxis so far. He was diagnosed as having a NSAIDs-induced urticaria/angioedema/anaphylaxis.

In conclusion, food allergy is the main cause of pediatric anaphylaxis but the remaining possible causes should not be ignored. A careful clinical history and the event diaries are very important tools for programming the diagnostic investigation. A drug hypersensitivity workup is necessary for diagnosis and to provide safe alternatives.

TP1273 | Formaldehyde IgE sensitization in Slovenian patients

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Background: Formaldehyde is a well-known allergen and is a common chemical substance found in a variety of applications. Apart from specific occupational exposures, the most frequent sources of exposures include skin and hair care products, cosmetics, certain cleaning products, medications, permanent press textiles and disinfectants. It is also used during dental treatment, especially for root canal disinfection. It usually causes contact dermatitis mediated by delayed-type hypersensitivity (Type-IV), however during dental treatment formaldehyde often causes immediate-type allergy (Type-I). The aim of our study was to explore formaldehyde sensitization and the culprit source of formaldehyde induced allergic reactions in our subjects, which were tested for formaldehyde IgEs in the last 20 years.

Method: Between 1998 and 2018, 301 subjects were examined in our hospital due to possible allergic reactions to formaldehyde. Clinical evaluation was done and formaldehyde-sIgE levels were assessed by Immulite 2000 assay for all subjects enrolled in a study. Positive results of formaldehyde-sIgE levels (≥0.35 kU/L) were compared to clinical data and clinical relevance of formaldehyde-sIgE was determined.

Results: Of all assessed subjects, formaldehyde-sIgE were detected in 59 (19.6%) subjects, the other part of the 242 subjects (80.4%) were formaldehyde-sIgE negative. Forty-nine of 59 formaldehyde sensitized subjects (83%) experienced allergic reaction few hours after dental treatment (median 3 hours; IQR 4 hours), and in the majority the symptoms were generalized urticaria and/or oedema. Other formaldehyde-sensitized subjects (10 of 59; 17%) showed no allergic symptoms. In 41 (69%) allergic patients the Toxavit was the cause of reaction and in eight (13.6%) Toxavit was a probable cause of reaction. In allergic patients, there was a trend of higher formaldehyde-sIgE levels (median 5.3 kU/L; IQR 15 kU/L) than in other formaldehyde sensitized subjects (median 1.8 kU/L; IQR 10.6 kU/L).

Conclusion: We showed that more than 80% of subjects IgE sensitized to formaldehyde demonstrate allergic reactions after exposure to formaldehyde during dental treatment. The major culprit was Toxavit, which is used to devitalise dental pulp, when endodontic surgical measures are not possible.

TP1274 | Propionic hypersensitivity and atopy: Relationship between severity and airborne sensitization

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Background: Propionic acid family is the most common NSAID used by our patients. Allergic rhinitis and asthma are the most frequent problems in our Allergy department, and no studies are published about airborne sensitization in propionic acid hypersensitivity. Our objective is to describe a population with propionic acid allergy confirmed in our Allergy Department and to evaluate airborne sensitization.

Method: Patients with propionic acid allergy diagnose were selected. After a clinical report, we performed skin prick test (SPT) with the main house dust mites, pollen, moulds and danders in our city. We performed a Drug Provocation Test with salicylate or with the culprit drug to exclude a cross-reactivity and to confirm the diagnose. Total IgE and specific IgE to aeroallergens were tested in some patients too. We compared the results according to drug severity.

Results: Seventy-eight patients (24 males and 54 females) were diagnosed. Sixty patients referred non-anaphylactic symptoms after drug intake (9 local angioedema, 14 urticaria, 10 urticaria-angioedema, 27 generalized angioedema) and 18 referred anaphylactic symptoms. Fifty-one patients referred allergic rhinitis (thirty-six (70%) in non anaphylactic group and 15 (83%) in anaphylactic group). SPT show us 21 positivities to D. pteronyssinus (12 (18.18%) in non anaphylactic group and 9 (50%) in anaphylactic group) or 13 to L. Perenne (5 (7.57%) and 8 (44.44%) respectively). These differences were significants ($P < 0.05$ and $P < 0.01$). No other differences were found in airborne sensitization in each group.

Conclusion: In our population, non-anaphylactic symptoms after propionic acid intake are more frequent than anaphylactic ones.

D. pteronyssinus and L. perenne sensitization are more frequent in anaphylactic group in comparison with non-anaphylactic group (significant differences)

More patients included in each group could show more statistical differences.

TP1275 | Promethazine anaphylaxis: A case report

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Case report: A 52 year old Caucasian man developed paresthesia, sweating, flushing and total paralysis a few hours after the use of promethazine for sea sickness. Two years later, he took Night Nurse (promethazine, paracetamol and dextromethorphan) as a sedative to help him sleep. An hour later, he developed a generalized erythematous rash with associated total paralysis. He subsequently developed a seizure while in the ambulance on the way to hospital. Since then he had tolerated the use of paracetamol.

Skin prick test (SPT) & intradermal test (IDT) were performed:

SPT: histamine 10 mm with flare; control: 0 mm; neat promethazine: negative

IDT: promethazine 1:10 - no weal expansion with 12 mm flare; 1:100 - negative

He then proceeded to an oral promethazine challenge. He received 10 mg promethazine in a graded fashion. He developed generalized erythema & pruritus together with urticaria on his abdomen. He suddenly became hypotensive and this was associated with limb tremors. He received adrenaline 0.5 mg intramuscularly and hydrocortisone 200 mg intravenously. The patient was transferred to the high dependence unit (HDU) for observation. However, the patient self discharged before a minimum of 6 hours of observation. The tryptase level was elevated at 20.8 µg/L.

Conclusion: Antihistamines are one of the commonest medications being used, especially for allergic conditions. Although it is exceedingly rare, one should be aware of the possibility of hypersensitivity reactions to anti-histamines. This is well illustrated by our case report which is likely to be the first reported case of an anaphylaxis to promethazine.

TP1276 | A true anaphylactic reaction from local anesthetics

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Case report: A problem that is encountered rather frequently is the suspected allergic reaction to local anesthetics. A very small number of these reactions happen due to an allergic mechanism, but most of them still remain unexplained.

Reports of adverse reactions to local anesthetics are usually attributed to a reaction to epinephrine, vasovagal syncope, or overdose toxicity, but many patients think this is caused by an allergy to local anesthetic. True allergy to amide local anesthetics is considered to be very rare, and it is thought that most reactions are pseudoallergy, and we must take into consideration that 80% of the reactions may be caused by antiseptic agents like paraben, methyl paraben and metabisulfite. Amide-type local anesthetics are metabolized in the liver and are essentially free from producing allergic phenomena.

It has been observed that lidocaine hydrochloride preparations have an especially high antigenicity, so local anesthetic allergy testing must be performed safely and with high accuracy.

Our patient, a 33-year-old female, came to our clinic to get tested for local anesthetic allergy. 2 years ago, during a dental procedure, she suffered from a systemic allergic reaction, Muller 3, after being injected with lidocaine and epinephrine. We preformed the intradermal injection test for Lidocaine HCl 2% diluted to 1:100, 1:10. The 1:10 test resulted significantly positive. Which was immediately followed by a severe anaphylactic reaction, Muller 4. The patient was treated in the ICU and after 2 hours of intensive treatment, she finally stabilized.

The dentist resubmitted the patient and asked us to test her for ester-type local anesthetics, but our team declined. Due to ester-type local anesthetics being out of the question, and the patient refusing the use of general anesthesia, the dentist decided to use 1% diphenhydramine with 1:100 000 epinephrine as an alternative local anesthetic.

The patient returned in our clinic to perform a complete allergic test. The in-vitro and in-vivo test resulted positive to some foods. This makes us believe that patients with past or current food allergies have a higher potential for the manifestations of the reactions.

TP1277 | Anaphylaxis to oral administration of a PEG laxative product confirmed with oral challenge

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Case Report:

Background: Polyethylene glycols (PEG) or macrogols are polymers widely used in drugs either as active substance (bowel preparations) or as excipient (e.g. antihistamines & corticosteroid injections). Moreover, they are ubiquitously found in additional medicinal and other products, such as cosmetics and food. Allergy to PEG shows an increasing trend, though relative awareness remains low. A case of well documented anaphylaxis to PEG and the allergological workup is presented.

Method: We report a 32 year old caucasian woman with anaphylaxis (throat pruritus, hoarseness, aphonia, palpitation, urticaria) that occurred immediately after oral intake of macrogol (13.3 g of 3350 MW) for constipation. The patient was treated with IV antihistamines and corticosteroids at the Emergency Dpt. 30 minutes later. The reaction subsided within 30 minutes and she fully recovered 6 hrs later.

Skin testings with the commercial preparation of the culprit PEG were performed 12 weeks after the reaction: SPT undiluted, IDs 1/10 000, 1/1000, 1/100 dilutions. Specific IgE quantification of ethylene oxide (ImmunoCAP®, Phadia ThermoFisherScientificInc) and basophil activation test (BAT) using $CCR3^+/CD63^+$ surface markers were also performed. Finally, a single-blind placebo-controlled oral challenge was conducted to determine reaction threshold using conventional protocol: 1/1000, 1/100, 1/10, 1/3 and the remaining of the full recommended dose every 30 minutes. A written informed consent was obtained by the patient.

Results: All skin tests were negative. However, 30 minutes after the 1/100 dilution ID injection, the patient developed few urticarial wheals at distant sites along with mild hoarseness while ENT endoscopy showed mild edema of the arytenoids. Serum tryptase after 2 hrs was 4.7 μg/L. Specific IgE was negative, while BAT turned strongly positive (stimulation index 4.00). Oral challenge was positive; an identical with the aforementioned after ID testing reaction occurred 30 minutes after the second dose (133 mg).

Conclusion: Anaphylaxis was well documented based on the clinical history combined with the positive BAT and the observed reactions during skin testings and oral challenge. However, an IgE mediated mechanism could not be proved, as skin testings and specific IgE were negative. Considering that the patient uses skin products with PEG excipients without reaction, we could speculate that either the oral route of administration or higher doses are needed for anaphylaxis occurrence.

TP1278 | Intraoperative anaphylaxis related to aprotinin after local application of fibrin sealant probably caused by an IgE-independent mechanism: A case report

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Case Report:

Introduction: Aprotinin is a serine protease inhibitor derived from bovine lung that has occasionally been reported as a causative agent of perioperative anaphylaxis. A case of anaphylaxis caused by aprotinin-containing fibrin sealant that was locally applied to the operation field during partial pulmonary resection is reported. Although many cases of aprotinin-induced anaphylaxis have been reported, few studies have investigated the underlying mechanism. In our view, this is the first report to suggest an IgE-independent mechanism for aprotinin-induced anaphylaxis using basophil activation tests (BATs).

Case: A 49-year-old woman underwent pulmonary surgery under general anesthesia. Written informed consent was obtained from the patient prior to the tests. Shortly after applying absorbable suture reinforcement felt made of polyglycolic acid that contained

fibrin sealant, her blood pressure fell to approximately 70 mm Hg, accompanied by facial flushing. Suspecting anaphylaxis, the felt was removed, and 0.3 mg of adrenaline was administered intramuscularly. Her general condition stabilized after these treatments. Based on the clinical symptoms and high serum tryptase levels, anaphylaxis was diagnosed. Three months after the event, skin tests with all agents including the felt and the fibrin sealant were performed. Skin tests showed positive results only for vial No. 2 of the fibrin sealant, whose main component is aprotinin. Subsequently, BATs with CD203c and CD63 were performed using serial dilutions of vial No.2 of the fibrin sealant and pure aprotinin. Wortmannin, an inhibitor of phosphoinositide 3-kinase, was used to investigate whether anaphylaxis was caused by an IgE-dependent or IgE-independent mechanism. Compared to a healthy control, the $CD203c^+$ basophils of the patient were significantly elevated by adding vial No.2 of the fibrin sealant and pure aprotinin to 35.7% and 35.4%, respectively. Similar results were obtained for $CD63^+$ basophils. These results demonstrated that the causative agent was likely aprotinin. The inhibitory effect of wortmannin on basophil activation by vial No.2 of the fibrin sealant and pure aprotinin was negligible, suggesting an IgE-independent mechanism underlying aprotinin-induced anaphylaxis.

Conclusion: Aprotinin-containing fibrin sealant may cause anaphylaxis through an IgE-independent mechanism. BAT may be useful to investigate the mechanism underlying drug-induced anaphylaxis.

TP1279 | A case of acetyl salicylic acid (ASA) induced asthma attack presented for first time after wine-asa mixture consumption in a young man with previous history of ASA anaphylaxis

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Case report:

Introduction: Acetyl Salicylic Acid - induced asthma (AIA) refers to the development of bronchoconstriction in asthmatic individuals following the ingestion of Acetyl Salicylic Acid (ASA). This syndrome encompasses classic symptoms of chronic rhinoconjunctivitis, nasal polyps, and asthma. The attacks may be precipitated following the ingestion of small amounts of ASA or other nonsteroidal anti-inflammatory drugs.

Case report: A 29 year old man not previously diagnosed for Asthma, was admitted in emergency department with severe dyspnea, wheezing, chest tightness, tachycardia, pallor and impossibility to speak because of dyspnea. Symptoms started 2 nights before with sneezing and dyspnea, which got worsen in time. The patient history showed that two nights before he drank homemade red wine "sweetened" with ASA. Patient referred that 10 years ago after ASA consumption he had swelling in the face and dyspnea, two days after this episode he self-tested taking another ASA tablet, which resulted in anaphylactic shock. Since there he avoided ASA and had no respiratory symptoms, no history for chronic rhinitis or nasal polyposis, but positive skin test for chicken and eggs since childhood, also allergic to penicillin and streptomycin.

Emergency examinations: Bilateral pulmonary wheezing, SPO_2 = 94%, RF = 23/min, CF = 120/min, AP = 130/90 mm Hg, EKG showed supraventricular tachycardia, chest radiography was normal, blood count normal values, urine examination normal, ERS = 12 mm/h, electrolytes and biochemical examinations were in normal ranges. Patient was immediately treated with O_2 therapy, Prednisolone 50 mg bolus IV and Dexamethasone 8 mg 20 drops/min IV. His conditions were significantly improved after 40 minutes and transferred to Allergy Department. Two hours later he had no wheezing in auscultation, less dyspnea. Spirometry conducted one day after showed normal ventilatory function. Two weeks later the patient conducted Bronchial Provocation Test with methacholine which resulted with > 20% fall in FEV1 values after inhalation of 4 mg/mL methacholine dose concentration.

Conclusions: This case present a rare severe AIA attack in a subject with no previous Asthma or respiratory problems history.

TP1280 | Outcomes of patients undergoing nasal aspirin desensitisation for aspirin exacerbated respiratory disease at lancashire teaching hospitals, a tertiary adult allergy centre in the UK

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Background: Aspirin-Exacerbated Respiratory Disease (AERD) consists of asthma, nasal and sinus polyps and a respiratory sensitivity to aspirin and non-steroidal anti-inflammatory drugs. Patients with this syndrome, often referred to as aspirin triad or Samter's triad, have progressive inflammatory disease of the upper and lower respiratory tracts. Aspirin desensitisation has been shown to be helpful with regards to the nasal symptoms these patients experience.

Method: The Drug Challenge Database maintained by the Allergy Department at Lancashire Teaching Hospitals was reviewed and all the notes of all the patients having undergone nasal aspirin desensitisation was reviewed. Outcome data with regards to improvement in the patient symptoms were collected.

Results: The data suggest that patients do benefit in having aspirin desensitisation, tolerate the procedure well and suffer with not much side effects.

Conclusion: Nasal aspirin desensitisation does have a role in helping patients with Aspirin Exacerbated Respiratory Disease.

TP1281 | CYSLTR2 genetic variants in nonsteroidal anti-inflammatory drug-induced urticaria/angioedema

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Background: Nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most highly consumed medicines worldwide, but they are also the main culprits in drug hypersensitivity reactions (DHRs). It is accepted that the inhibition of the cyclooxygenase-1 (COX-1) enzyme shunts the arachidonic acid metabolism towards the synthesis of cysteinyl-leukotrienes (CysLTs), which in turn elicit a DHR in susceptible individuals after its interaction with specific receptors. Genetic susceptibility to DHRs to NSAIDs has been mainly evaluated in patients with NSAIDs-exacerbated respiratory disease (NERD) even if NSAIDs-induced acute urticaria/angioedema (NIUA) is the most frequent clinical entity induced by DHRs. Variants in the CysLT receptor 2 gene (*CYSLTR2*) have been associated with both asthma and NERD; however, there is a lack of studies concerning their potential involvement in NIUA. The aim of this study was to evaluate the overall genetic variability in the *CYSLTR2* gene in NIUA patients.

Method: A total of 240 NIUA patients and 312 healthy controls with no significant age and sex differences were included. We selected a set of 5 tagging single nucleotide polymorphisms (tSNPs) in *CYSLTR2*, using European population's data available from the 1000 Genomes Project. Genotyping was performed using the iPlex Sequenom MassArray technology.

Results: One tSNP in the 3′-UTR region of the *CYSLTR2* gene (rs2407249) was found to be statistically associated with a diminished risk of NIUA after Bonferroni multiple testing correction according to the additive model (corrected *P*-value of 0.045; OR: 0.67, CI: 0.5-0.9). This variant was also marginally associated with NIUA after other models of inheritance (codominant, dominant, and recessive).

Conclusion: Our results suggest a role for the rs2407249 *CYSLTR2* genetic variant in NIUA, the most frequent entity induced by DHRs. Further studies are required to replicate these associations, to evaluate the potential participation of *CYSLTR2* variability in other entities induced by hypersensitivity to NSAIDs and to shed light on the molecular basis underlying this association.

TP1282 | Nonsteroidal anti-inflammatory drug hypersensitivity in patients with clonal mast cell disorders – an exaggerated risk?

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Background: Several reports have shown an increased risk for anaphylaxis and other hypersensitivity reactions in patients with clonal mast cell disorders (cMCD) and a strong association has been established in patients with venom-induced anaphylaxis or unexplained anaphylaxis. It is therefore hypothesized that these patients may even predispose systemic hypersensitivity reactions to certain drugs including non-steroidal anti-inflammatory drugs (NSAID). Since there has been a lack of studies to generate clear recommendations, these patients have been discouraged to use this kind of drugs. The aim of the current study was sought to determine the actual prevalence and severity of NSAID-related hypersensitivity reactions among patients with cMCD.

Method: A retrospective study was conducted among 202 (≥18 years old) consecutive patients who were diagnosed with mastocytosis (n = 169) or monoclonal mast cell activation syndrome (MMAS) (n = 33) in the Mastocytosis Center Karolinska from January 2006 to December 2018. A thorough allergy work-up including the clinical evaluation of self-reported NSAID-induced hypersensitivity reactions was performed for each individual patient. All enrolled patients were provided their written informed consent to participate.

Results: Of the patients, 18 (8.9%) were identified with suspected NSAID hypersensitivity. Most patients reacted with cutaneous symptoms (89%), whereas 4 (22%) patients had anaphylactic reactions. NSAID hypersensitivity was reported with slightly higher frequency in the MMAS (15.2%) patients compared to patients with mastocytosis (7.6%), although this was not significant. All NSAID-related hypersensitivity reactions were experienced before cMCD were diagnosed. There was no difference between the groups regarding atopic status, although IgE levels were slightly higher in patients with MMAS.

Conclusion: The overall prevalence of NSAID hypersensitivity was determined to be 8.9% in our cohort, which indicates about a 4-fold increased risk compared to the general population. However, most NSAID reactions were limited to skin as the prevalence of anaphylaxis was 1.9% in overall. Our preliminary results suggest that cMCD patients without history of NSAID may be treated with NSAID without special precautions.

TP1283 | A single NSAID-induced anaphylaxis to diclofenac, confirmed by skin testing

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Case report: Nonsteroidal anti-inflammatory drugs (NSAIDs) are a major culprit of drug-induced hypersensitivity. No reliable diagnostic tests other than a direct challenge are available. Cross-reactivity among NSAIDs that inhibit cyclooxygenase-1 is common. However, in rare cases, the mechanism underlying hypersensitivity is immunologically understood, without involving cross-reactivity of NSAIDs, or even with a positive skin test for an NSAID.

A 55-year-old woman was referred to the emergency department for anaphylaxis. She suffered from generalized hives, chest tightness, and hypotension a few minutes after intramuscular diclofenac injection. One year before, she had experienced a similar reaction after intramuscular injection of aceclofenac. Thereafter, she had been taking naproxen as needed to relieve her osteoarthritis pain, without having an adverse reaction.

To confirm drug hypersensitivity and to find alternative drugs, provocation tests were performed with acetaminophen, celecoxib, and lysine-aspirin. All tests were negative, and a skin prick test with diclofenac was also negative. However, intradermal injection of 0.05 cc (37.5 mg/mL) diclofenac provoked an anaphylactic shock and resulted in her admission.

Here, we report a rare case of single NSAID-induced anaphylaxis, which was only triggered by acetic acid derivatives of NSAIDs, presumably by an immunoglobulin E-mediated reaction.

TP1284 | Selective-allergic reaction to heteroaryl-acetic acid derivates

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Case report: Non-steroidal anti-inflammatory drugs (NSAIDs) are becoming increasingly responsible for a higher prevalence of hypersensitivity reactions. Selective reactions differ from those that occur in cross-reactive ones in that good tolerance exists to the remaining NSAIDs, even if they share the same COX1 inhibitor mechanism. Thus, a culprit drug may be safely substituted with another NSAID with different chemical structure but similar anti-inflammatory potency.

47-year-old woman, diagnosed with rheumatoid arthritis since 2001 and medicated with methotrexate, proglumetacin and deflazacorte for the last two months. Several years before being referenced to allergology consultation she took 100 mg diclofenac; two hours after she experienced a mild generalized urticaria, which subsided spontaneously. Five months before the consultation, she took 100 mg aceclofenac and thirty minutes after she had generalized urticaria, facial/labial edema, sensation of tightness in her throat, shortness of breath and lipothymia. The reaction subsided in the next hour and a half after the administration of intramuscular epinephrine, hydrocortisone and clemastine. She had previously taken paracetamol and kept taking proglumetacin with good tolerance. There was no personal or family history of atopy. At consultation she underwent controlled oral provocation test with nimesulide which was negative and then with acetylsalicylic acid, also negative, to exclude cross-reactive type of hypersensitivity. In the meanwhile she was administered an intravenous injection of metamizol without any reaction. Oral challenge with etodolac was also performed which was also negative and confirmed tolerance to indol-acetic acid derivates (such as proglumetacin). Selective COX-2 inhibitors were not tested.

Although cross-reactive reactions are the most frequent among NSAID hypersensitivity reactions, a significant proportion of them are selective reactors with an IgE-mediated mechanism proposed with different degrees of evidence. No well validated cutaneous diagnostic tests are available, and the diagnosis is made through drug provocation tests with an alternative or culprit drug.

This patient has a selective allergic reaction to heteroaryl-acetic acid derivates (diclofenac and aceclofenac), but she tolerates indol-acetic acid derivates, both of which belong to the same NSAIDS chemical class and are distinguished only by a radical group. She also tolerates all the other chemically unrelated NSAIDs.

TP1286 | Allergy to a NSAID arylpropionic acid derived and tolerance to other NSAID aril-propionic

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Case report: Nonsteroidal anti-inflammatory drugs (NSAIDs) represent one of the most frequent causes of drug-induced urticaria/angioedema worldwide. Immediate hypersensitivity reactions to a single NSAID or to several NSAIDs belonging to the same chemical group, manifested as urticaria, angioedema and/or anaphylaxis and the most frequent NSAIDs involved are pyrazolones, ibuprofen, diclofenac, ASA and paracetamol. These subjects tolerate other chemically nonrelated NSAID and do not have a history of chronic urticarial or asthma. The ibuprofen and dexketoprofen are a propionic acid group of NSAID. It is a COX-1 and COX-2 inhibitor with well-known anti-inflammatory and analgesic effects. We present two cases of patients with hypersensitivity and tolerance to NSAIDs arylpropionics derived structurally related.

Background: Nonsteroidal anti-inflammatory drugs (NSAIDs) represent one of the most frequent causes of drug-induced urticaria/

angioedema worldwide. Immediate hypersensitivity reactions to a single NSAID or to several NSAIDs belonging to the same chemical group, manifested as urticaria, angioedema and/or anaphylaxis and the most frequent NSAIDs involved are pyrazolones, ibuprofen, diclofenac, ASA and paracetamol. These subjects tolerate other chemically nonrelated NSAID and do not have a history of chronic urticarial or asthma. The ibuprofen and dexketoprofen are a propionic acid group of NSAID. It is a COX-1 and COX-2 inhibitor with well-known anti-inflammatory and analgesic effects. We present two cases of patients with hypersensitivity and tolerance to NSAIDs arylpropionics derived structurally related.

Method: The first patient was an 18 year-old woman who presented generalized itchy wheals and angioedema during 30 minutes after 6 hours after taking 550 mg of naproxen. She had no history of cutaneous disease and had subsequently tolerated 600 mg of ibuprofen.

The second case was a 40 year-old woman who after 1 hour taking 600 mg ibuprofen presented generalized itchy wheal. She had no history of cutaneous disease and had subsequently tolerated 25 mg of dexketoprofen

Single Blind Placebo Controlled Oral Challenge (SBPCOC) was performed on the first patient with naproxen (doses of 100, 150 and 300 mg, administered at 90-min intervals) and ibuprofen (doses of 100, 200 and 300 mg were administered the first day at 90-min intervals, and a single dose of ibuprofen 600 mg was administered a second day). Dexketoprofen (doses of 12.5, 12.5 and 25 mg) and ibuprofen was carried on the second patient at the same intervals.

Results: The SBPCOC of the first patient was negative to ibuprofen and positive to naproxen (itchy wheals after the doses of 150 mg)

The SBPCOC of the second patient was negative to dexketoprofen and positive to ibuprofen (itchy wheals after the dosis of 200 mg)

Conclusions: We have demonstrated a selective reactivity to a NSAID arylpropionic acid derived with tolerance to another NSAID of the same group. Cross reactivity should not be assumed within the same group.

TP1287 | Risk factors for developing positive lysine-aspirin nasal challenges in non-steroidal anti-inflammatory drugs (NSAIDs)-exacerbated respiratory disease

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Background: Non-steroidal anti-inflammatory drugs (NSAIDs)-exacerbated respiratory disease (NERD) is defined as hypersensitivity reactions induced by aspirin (ASA) or other NSAIDs manifesting as bronchial obstruction, dyspnea, and nasal congestion/rhinorrhea, occurring in patients with an underlying chronic airway respiratory disease (asthma/rhinosinusitis/nasal polyps). A drug provocation test (DPT) can be needed to confirm the diagnosis, being nasal provocation test with lysine-aspirin (NPT-LASA) safer and faster to perform than the oral. Our aim was to evaluate the factors related to a positive response in NPT-LASA.

Method: NPT-LASA was carried out in 57 confirmed NERD cases (≥3 episodes of respiratory symptoms induced by ≥ 3 NSAIDs non-chemically related or positive oral DPT with ASA) and in 30 tolerant subjects to NSAIDs. We analyzed clinical features of patients (age, gender, underlying diseases, atopy, smoking habit), as well as number of episodes, symptoms induced by NSAID, time interval between drug intake and reaction onset and between last reaction and study in both negative and positive NPT-LASA cases.

Results: The 73.7% of NERD subjects were female of 42.5 (25.75-55.25) years and 66.7% non-smoker. The 66% were atopic, 70.4% had underlying rhinitis, 63% asthma and 30.2% polyposis. Regarding symptoms experienced after NSAIDs intake, the 52.7% developed asthma, 30.9% rhinitis/asthma, 5.4% throat tightness/asthma and 3.64% rhinitis and/or throat tightness. NPT-LASA was positive in 45 patients, but in no controls, being sensitivity 78.94% and specificity 100%. The 50% of patients with positive NPT-LASA had nasal polyposis whereas this percentage was 11.1% in those with negative NPT-LASA ($P = 0.002$, OR = 8 (1.923-33.274), $P = 0.004$).

Conclusion: NPT-LASA shows a high sensitivity and specificity for diagnosing NERD. The risk for developing a positive NPT-LASA was 8 times higher if patient had nasal polyposis.

TP1288 | Is etoricoxib a safe long term alternative in patients with NSAIDs hypersensitivity reactions?

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Background: Nonsteroidal anti-inflammatory drugs (NSAIDs) are the most frequently prescribed drugs in medical practice. Patients who have hypersensitivity reactions (HSR) are very limited in their analgesic and anti-inflammatory therapeutic options, but several studies have shown that cyclooxygenase-2 (COX-2) inhibitors can be safely used. However, there are no studies on long term tolerance.

Objective: To assess if patients with HSR to NSAIDs maintained tolerance to COX-2 inhibitors that was previously confirmed by an oral challenge (OC).

Method: Patients with NSAIDs HRS submitted to an OC with etoricoxib between 2015 and 2017 in our Drug Allergy Unit were selected. A medical records review and a telephone survey was conducted to evaluate long term tolerance.

Results: A total of 67 patients were included, 46 (69%) female and 21 (31%) male, with a mean age of 45 (±13) years. Ibuprofen and aspirin were the most frequent culprit NSAIDs.

The main manifestations were cutaneous symptoms in 29 (43%) patients, respiratory symptoms in 11 (16%), 9 (14%) had skin and gastrointestinal symptoms and 18 (27%) had anaphylaxis.

With respect to comorbidities, 24 (36%) patients had asthma or urticaria and of these 18 (75%) reported worsening of their symptoms with NSAIDs. Information on long term tolerance was obtained in 47(70%) patients. Of these, 23 (49%) denied taking etoricoxib again: eleven (48%) did not require it; 7 (30%) did not understood that the drug was a safe alternative and 5 (22%) were still afraid of a reaction. Of the remaining 24 (36%) who continued to take etoricoxib, only one reacted 22 months later with asthma exacerbation.

Conclusion: This study confirms that Cox-2 inhibitors are safe in patients with hypersensitivity reactions to Cox-1 inhibitors but we still need to highlight this in order that this message is clearly understood by the patients.

TP1289 | Nimesulide tolerance assessment in patients with non-selective non-steroidal anti-inflammatory drugs hypersensitivity

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Background: Non-selective non-steroidal anti-inflammatory drugs (NSAIDs) hypersensitivity is the predominant type of drug hypersensitivity in Latin America. The suggested mechanism involves COX-1 inhibition, and patients usually react to multiples NSAIDs. This study aimed to assess tolerance to nimesulide, a COX-2 preferential inhibitor, in these patient

Method: Patients with at least two reactions to two chemically different NSAIDs that showed tolerance to etoricoxib were invited to participate in the study. After their consent, a single-blinded drug provocation test (DPT) started with placebo and followed by 10% and 90% of the therapeutic nimesulide dose was performed, with a one-hour interval between drug doses. The DPT was positive when the patient replicated the original symptoms within 24 hours after the last dose. All the patients remained under observation for two hours after the end of the procedure. Those who reacted were adequately treated

Results: Twenty-eight patients were included in the study (68% female, mean age 37 ± 19.8 years). Twelve (43%) had a history of a severe reaction, and in 79% the symptoms started within one hour of the drug intake. A positive DPT was observed in three patients (11%). Two had isolated angioedema and one anaphylaxis and were treated with antihistamines and adrenaline plus antihistamines, respectively, with total recover in less than two hours. None of the other twenty-five patients had symptoms within 24 hours after being discharged from the hospital.

Conclusion: Nimesulide has shown to be a safe alternative in patients with non-selective NSAIDs hypersensitivity. A DPT is mandatory to check tolerance before prescribing the drug for these patients.

MONDAY, 3 JUNE 2019
TPS 39
IMMUNOTHERAPY II: CLINICAL FOCUS

TP1290 | Effectiveness and safety of a modified Dermatophagoides Pteronyssinus allergoid, associated with microcrystalline tyrosine, in adult patients with allergic rhinitis, with or without asthma

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Background: An extract of *D. Pteronyssinus* modified with glutaraldehyde and associated with MCT has exhibited tolerance and effectiveness in a preliminary study with 30 patients. The objective of this new study, developed under normal clinical practice conditions, is to obtain further results of efficacy and safety.

Method: The present study was a prospective, observational and multi-centre study developed in adult patients with allergic rhinitis caused by the house dust mite *Dermatophagoides pteronyssinus (DP)*, who received immunotherapy with a glutaraldehyde-modified, MCT-associated extract of DP 100% for 1 year. The primary endpoint was the combined symptoms and medication score (CSMS). Secondary endpoints were symptoms score (SS), medication score (MS), % of well and bad days, ARIA classification and rhinitis control.

Results: Out of 141 patients recruited, 118 could be evaluated. 57% were women with an average age of 34 years. There were significant changes in the different evaluated variables after 6 months of treatment, compared with the baseline. These differences persisted until 1 year of treatment ($P < 0.01$): CSMS −43%; SS −41%; MS −51%. % well days from 46.4% (baseline) to 65.5% (1 year); % bad days, from 15% (baseline) to 7.1% (1 year). Persistent symptoms (ARIA) from 79.7% (baseline) to 15.5% (1 year); moderate/severe (ARIA) from 83.1% (baseline) to 20.2% (1 year); controlled rhinitis from 7.6% (baseline) to 63.1% (1 year). A total of 18 patients (15.3%) experienced a total of 88 adverse events: 83 (95.4%) local reactions at injection site and 4 (4.6%) and 4 mild systemic reactions (discomfort, headache, nasopharyngitis).

Conclusion: An extract of *D. Pteronyssinus* modified with glutaraldehyde and associated with MCT, in patients with allergic rhinitis caused by *Dermatophagoides*, is safe and shows significant clinical improvement in all analysed variables, at 6 and 12 months after treatment.

TP1291 | Results of immunotherapy with a polymerized extract associated with microcrystalline tyrosine, in patients with allergic asthma caused by the house dust mite dermatophagoides

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Background: A house dust mite extract modified with glutaraldehyde and associated with microcrystalline tyrosine [MCT]) has previously exhibited tolerance and effectiveness in patients with allergic rhinitis caused by *Dermatophagoides pteronyssinus*. The objective of this sub-analysis was to evaluate the effectiveness of the treatment in a subgroup of patients with bronchial asthma.

Method: This trial was a prospective, observational and multi-centre study, developed in adult patients with allergic rhinitis, with or without asthma, caused by *Dermatophagoides*, who received immunotherapy (*D. pteronyssinus* [DP] 100%), for 1 year. In the group with bronchial asthma the following variables were analysed at baseline, after 6 months and 1-year post-treatment: % of days with symptoms, % of days with medication, GEMA classification and quality of life (AQLQ).

Results: Fifty-five (46.6%) out of 118 evaluated patients had bronchial asthma (average disease duration 14.1 years). A significant reduction was observed ($P < 0.05$) in the % of days with symptoms (baseline: 23.9%; 6 months: 11.7%; 1 year: 5.1%) and in the % of days with medication (baseline: 67.6%; 6 months: 49.5%; 1 year: 45.1%). According to GEMA classification, the % of patients with persistent asthma changed from 78.2% (baseline) to 38.9% (1-year post-treatment) ($P = 0.008$). The total score of the quality of life changed from 3.03 (baseline) to 1.23 (6 months) and 1.45 (1 year) ($P < 0.0001$).

Conclusion: Patients with bronchial asthma, caused by allergy to *Dermatophagoides*, treated with an allergoid of *D. Pteronyssinus* associated with MCT exhibited a significant clinical improvement (reduction of days with symptoms, days with medication and GEMA classification) and improvement in their quality of life after 6 and 12 months of treatment.

TP1292 | Improved quality of sleep in allergic rhinitis patients treated with house dust mite SLIT-tablet

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Background: Poor sleep, both quality and less time spent sleeping, is one of many bothersome consequences of being affected by allergic rhinitis, with potential great impact on both personal life and societal contribution. House dust mite (HDM) SLIT-tablet (12 SQ-HDM, ALK, Denmark) has been shown to be effective in treating HDM allergic rhinitis and asthma in several large DBPC trials. This post-hoc analysis investigates treatment effect with HDM SLIT-tablet on sleep in HDM allergic rhinitis patients.

Method: Subjects from a Phase III trial (EudraCT: 2011-002277-38; placebo: N = 338, 12 SQ-HDM: N = 318) with moderate-severe HDM allergic rhinitis (defined as: a daily total rhinitis symptom score of at least 6 or a score of at least 5 with 1 severe symptom during at least 8 days of the 15-day baseline period) were treated for up to 1 year (Demoly et al. 2016;JACI;137:444-51). At baseline and during the course of the trial each subject filled-in Juniper's RQLQ, evaluating 3 sleep parameters (Difficulty getting to sleep, Wake up during night, Lack of a good night's sleep) with scores from 0 (not troubled) to 6 (extremely troubled). For the purpose of this analysis, scores < 3 were categorized into "mildly affected" and ≥ 3 into "moderately/severely affected". Sleep scores during baseline and efficacy assessment period at the end of the trial were used.

Results: Of those moderately/severely affected on sleep parameters at baseline (62-72% of the population) only 7-10% remained in that category following treatment with the SQ-HDM tablet (see Table). This improvement was significantly higher than that observed following treatment with placebo. For those starting in the mild category, 1-7% shifted to the moderate/severe category at end-of-treatment with no difference between placebo and 12 SQ-HDM groups (see Table).

Conclusion: Treatment with 12 SQ-HDM significantly improved quality and quantity of sleep for the group of patients who were affected by poor sleep at baseline.

TP1293 | Long-term effect of aeroallergens sublingual immunotherapy in allergic rhinitis and asthma patients

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Background: The management of Allergic Rhinitis (AR) with concomitant asthma is mainly pharmacologic; sublingual immunotherapy (SLIT) has been proposed as a disease-modifying option. Its long-term effect is still being evaluated. To assess the efficacy and long-term effect of aeroallergens SLIT in AR and asthma.

Method: This is a retrospective chart review study at our tertiary allergy clinic from 2007 onwards, including all AR/asthma patients who initiated SLIT (T0) for a 36 months period (T1). A subgroup of patients was evaluated 2 years post-SLIT (T2). Asthma symptom score (ASS), rhinitis total symptom score (RTSS), asthma medication consumption score (AMCS) and rhinitis medication consumption score (RMCS) were measured at T0, T1 and T2. Wilcoxon test compared outcomes between T0 and T1 and Friedman test assessed the sustainability of results at T2. Spearman's correlation evaluated the correlation of the outcomes with age.

Results: A total of 174 patients were included, 27% younger than 12 years old, 47.1% females, and 26.4% polysensitized. Follow-up at 36 months was complete, and 47 patients were assessed at T2. At T1, AMCS significantly improved from median 6 to 1 ($P < 0.05$), ASS from 3 to 1 ($P < 0.05$), RTSS from 14 to 6 ($P < 0.05$) and RMCS from 4 to 3 ($P < 0.05$). At T2, these results were maintained with RTSS 6($P < 0.05$) and RMCS 3 ($P < 0.05$), but not for AMCS and ASS. In the subset of patients who reached T2, polysensitized patients and children younger than 12 years old seem to have lost long-term efficacy based on AMCS assessment at T2 ($P < 0.05$). Subjects monosensitized to dust mites and not pollen retained long-term efficacy at T2 ($P < 0.05$) based on AMCS at T2.

Conclusion: SLIT significantly alleviates AR and asthma symptoms and reduces medication score in AR and asthmatic allergic patients after 3 years of therapy. Its long-term disease-modifying effect in asthma, 2 years after completing a three-year course, is only found in a subgroup older than 12 and monosensitized to dust mites. Larger prospective studies should be considered to better confirm our findings.

Sleep status at Baseline		Moderate/severe at End-of-Trial Placebo (%)	Moderate/severe at End-of-Trial 12 SQ-HDM (%)	*P* -value
Moderate/severe	Difficulty getting to sleep	17.2	7.3	0.006
	Wake up during night	23.0	8.4	<0.001
	Lack of a good night's sleep	27.5	10.1	<0.001
Mild	Difficulty getting to sleep	6.6	5.4	0.778
	Wake up during night	2.5	1.1	0.519
	Lack of a good night's sleep	4.3	3.9	0.908

TP1294 | Long-term clinical effectiveness of sublingual immunotherapy in allergic rhinitis

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Background: Allergen immunotherapy (AIT) in patients with allergic rhinitis (AR) has proven to have disease - modifying effect and clinical benefits that last after treatment's discontinuation. However, data on long-term effectiveness of sublingual immunotherapy (SLIT) on symptom control is insufficient. The *aim* of our study was to investigate sustained effectiveness of grass and house dust mite (HDM) SLIT on AR control five years after treatment.

Method: A total number of 50 AR patients with or without asthma [28 (58%) male; 30 (60%) with grass pollen SLIT and 20 (40%) with HDM SLIT] who were well-controlled after a three- or four-year course of SLIT, were prospectively evaluated on the fifth year after discontinuation of therapy. Mean age of patients was 31.96 years [SD 1.4; age range 17-55]. Out of all patients, 27 (54%) underwent a three-year SLIT course and 23 (46%)- a four-year SLIT course. Control of disease was assessed by Rhinitis Control Assessment Test (RCAT).

Results: When assessed on the fifth year, 44 (88%) of all patients were well controlled- 24 (80%) from the grass SLIT group and 20 (100%) from the HDM SLIT group. We found no significant difference between the number of well-controlled patients in the three- and the four-year SLIT group [$t = 1.78$ ($P > 0.05$)]. Additionally, we evaluated the appearance of newly diagnosed asthma. It was established in only one patient (2%).

Conclusion: SLIT with either grass pollen or HDM seemed to have at least a five-year effect on symptom control in patients with AR. We demonstrate that a three-year SLIT course has an effectiveness equal to the four-year one.

TP1295 | Evaluation of the long-term effect of allergen immunotherapy in local allergic rhinitis patients

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Background: Several randomized double-blind placebo-controlled trials have demonstrated the beneficial clinical effect of allergen immunotherapy (AIT) in improving symptoms, medication requirements and quality of life of local allergic rhinitis (LAR) patients. This study intends to investigate two new aspects: 1: the long-term clinical effect of AIT after its discontinuation; 2: the capacity of AIT to prevent asthma onset in LAR patients.

Method: Objective 1: two-year prospective study of 19 LAR individuals who satisfactorily responded to three-year treatment with grass-AIT. Objective 2: comparative study of the previous individuals (AIT group) and LAR patients not receiving AIT (not-AIT). An assessment of the clinical state, asthma presence, use of rescue medication, visits to the emergency department, quality of life (RQLQ), and a nasal allergen provocation test (NAPT) were performed at baseline (the moment of AIT discontinuation in the treated group) and two years later.

Results: Two years after AIT discontinuation, 94.7% of patients in the AIT group maintained a similar/better clinical state, 89.5% showed a similar/lesser consumption of rescue medication, 73.7% reported a similar/better RQLQ ($P > 0.05$), and there was an increase in the concentration of allergen tolerated in the NAPT. During the study period, 25% of not-AIT patients required visits to emergency department and 11.9% developed asthma, whereas no visit or asthma cases occurred in the AIT group ($P < 0.001$).

Conclusion: Three years of grass-AIT induces a long-term clinical effect on LAR, which persists after therapy discontinuation, and prevents asthma. This effect might be related to the achievement of immunological tolerance.

TP1297 | Safety and utility of rush immunotherapy with aqueous allergen extracts for the treatment of respiratory allergies

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Background: Allergen immunotherapy (AIT) needs long-term treatment duration to alter the natural course of allergy. Rush immunotherapy (RIT) shortens the duration of initial build-up phase and improves convenience compared with conventional immunotherapy (CIT). However, RIT has been usually performed with modified allergens such as allergoids or depot adjuvants. This study aimed to investigate the safety and utility of RIT with aqueous allergen extracts.

Method: We reviewed medical records of patients who have taken subcutaneous AIT with aqueous allergen or aluminum hydroxide adsorbed depot allergen for allergic rhinitis and/or asthma. They were divided into 3 groups: group A (n = 36, mean age 25.6 ± 13.4 years) received RIT with aqueous allergen; group B (n = 25, 27.2 ± 13.4 years) received RIT with depot allergen; group C (n = 22, 27.8 ± 14.1 years) received CIT with aqueous allergen. Patients treated with AIT targeting only house dust mite were excluded.

Results: Mean allergen numbers mixed in AIT was 3.7 ± 1.0, 3.1 ± 1.1 and 3.4 ± 1.1, in group A, B and C, respectively. Mixed allergens were house dust mite (80.6%), tree pollen (61.1%), animal

dander (58.3%), weed pollen (19.4%) and grass pollen (2.8%) in group A which was comparable with group C. In group B, proportions of grass (20.0%) and weed pollen (48.0%) were higher and that of animal dander (16.0%) was lower, compared with group A and C. Mean injection numbers during build-up phase was 14.1 ± 1.1, 17.0 ± 0.2 and, 14.2 ± 1.4 in group A, B and C, respectively ($P < 0.001$). Number of outpatient clinic visit decreased to 2.1 ± 1.4 and 1.0 ± 0.2 in group A and B, respectively, compared with 13.3 ± 2.9 in group C ($P < 0.001$). Build-up phase decreased to 25.0 ± 11.3 days and 17.4 ± 1.8 days, in group A and B, respectively, compared with 88.2 ± 17.8 days in group C ($P < 0.001$). Proportion of patient experienced systemic reaction increased to 77.8% and 80.0% in group A and B, respectively, compared with 31.8% in group C ($P < 0.001$). Mean number of systemic reaction per patient increased to 2.0 ± 1.9, 1.4 ± 1.0 in group A and B, respectively, compared with 0.5 ± 0.8 in group C ($P = 0.001$).

Conclusion: Rush immunotherapy with aqueous allergen was found to reduce frequent hospital visit and duration of build-up phase as well as to offer comparable safety with aluminum hydroxide adsorbed allergen. AIT with aqueous allergen extract can be widely applied to patients with respiratory allergies.

TP1298 | Peanut content of chocolate coated peanut candies present a higher variability when compared to conventional peanuts

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Background: Commercial chocolate covered peanuts with candy shells have emerged as a convenient and palatable option for oral immunotherapy. However, the consistency of peanut content between candies has never been assessed. The aim was to determine the consistency of peanut content included in chocolate covered candies and compare it with whole roasted peanuts in the context of peanut oral immunotherapy.

Method: Candies from a common international brand were visually assessed for size and shape prior to the manipulations to imitate parent's practice. They were then weighed, and chocolate coating was melted in the microwave. Peanut content was isolated using mild pressure and hot water. The number of peanut halves contained in each candy was documented and weighed separately. Correlation between the initial candy weight and peanut content was assessed with Pearson correlation coefficient (Pearson's r). Whole roasted peanuts from another common international brand were used as controls and submitted to the same characterization and measurements. Descriptive analysis as well as comparison of variability between chocolate covered peanuts and whole roasted controls were performed with SPSS.

Results: A total of 302 consecutive candies were evaluated. Of these, 23 were characterized but rejected on the basis of their abnormal shape or size. The mean peanut weight of the remaining candies was 588 mg (±140 mg) and followed normal distribution. Two candies contained no peanut halves, three contained one half, two contained three halves and one contained four halves. Correlation between the initial candy weight and peanut content was low (R^2=0.13). Whole roasted peanuts (n = 100) were significantly bigger (854 ± 139 mg; $P < 0.0001$) and all contained two halves. The variability of peanut content relative to the expected mean was greater for peanut candies (18% ± 15) than for roasted peanuts (12% ± 11) ($P = 0.0002$).

Conclusion: There is a high variability in peanut weight within each type of peanut presentation. Chocolate coated peanut candies use smaller peanuts than what was found in the commercial whole roasted peanut. The relative variability between each candy was also greater than the relative variability between whole roasted peanuts. This should be taken into consideration when counselling patients on peanut oral immunotherapy to ensure dosing consistency within desired parameters.

TP1299 | Cow's milk oral immunotherapy – characterization of our population

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Background: The aim of the study was to characterize our patients with cow's milk allergy (CMA) who underwent cow's milk oral immunotherapy (CM OIT).

Method: Retrospective analysis of the files of patients who performed CM OIT over a 10-year period (2008-2018). Before OIT, a positive oral provocation test or a consistent CM allergic reaction in the last year was needed.

Results: We included 44 patients (24 females) with CMA diagnosis, who started CM OIT at a median age of 8.9 years (1-20 years). We used a cluster protocol in 33 patients, with the need of slower doses' increases in 13 of them. The other 11 patients went through personalized protocols, that included baked milk, yogurt and CM small dose increments at home. The target dose was 200 mL/day. Symptoms occurred in 36 (82%) patients during OIT: 61% mucocutaneous, 61% gastrointestinal, 42% respiratory and 28% anaphylaxis. Most of the reactions were associated with doses' increases. Most of the children (59%) are in the maintenance phase (n = 26), 4 are in the up-dosing phase and 32% dropped off (n = 14). Twenty-five patients (of the 26) reached the target dose (10.3 months on average) and one eats baked milk. We followed them for 2.7 years on average: 14 reached a CM diet without restrictions, 10 maintain

tolerance to 200 mL of CM daily, at least, 1 reduced to 150 mL/d and 1 eats baked milk with no restrictions. Eight of the patients who finished OIT had symptoms during the maintenance phase. Considering the patients who interrupted OIT, all of them had symptoms during OIT. This was referred as the main reason for stopping the procedure (n = 8), followed by a difficult patient/family collaboration (n = 5). In 1 patient, the interruption was due to the appearance of eosinophilic esophagitis. All patients had positive specific IgEs before the start of OIT, presenting an average of 49.8 KU/L CM proteins, 20.7 KU/L α- lactalbumin, 10.7 KU/L β-lactoglobulin and 47.7 KU/L casein.

Conclusion: In our sample, OIT was successful in 2/3 of patients. It is a very demanding procedure with an elevated risk of associated reactions, so it must be performed in specialized centres. To increase the success rate of OIT we think that, before starting OIT, the candidates must be carefully chosen and the need to a psychological counselling during the process must be assessed. Also, we still lack evidence about the best age to start this approach to a CMA patient.

TP1301 | Safety of ultra-rush schedule of subcutaneous allergen immunotherapy with house dust mite extract conducted for 8 hours in an outpatient clinic in patients with allergic rhinitis

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Background: Ultra-rush schedule of subcutaneous allergen immunotherapy (UR-SCIT) administering maximum maintenance dose of allergen extract within one day can save time and effort in patients with allergic diseases. However, UR-SCIT is associated with an increased risk of systemic reaction (SR) compared to conventional subcutaneous allergen immunotherapy and is usually conducted in a hospital admission setting. To overcome these limitations of UR-SCIT, we evaluated the safety of UR-SCIT conducted in an outpatient clinic in patients with allergic rhinitis.

Method: UR-SCIT was performed in 26 patients with allergic rhinitis and hypersensitivity to house dust mites (HDM). A maximum maintenance dose of tyrosine-adsorbed HDM extract (1 mL of maintenance concentration) was divided into 4 increasing doses (0.1, 0.2, 0.3, and 0.4 mL) and administered to the patients by subcutaneous injections at 2-hour interval for 8 hours in an outpatient clinic. SR associated with UR-SCIT was classified according to the World Allergy Organization grading system.

Results: SR was observed in 3 of 26 patients (11.5%) during UR-SCIT. Observed SR was grade 1 in one patient (3.8%), grade 2 in one patient (3.8%), and grade 3 in one patient (3.8%). Grade 4 SR or grade 5 SR was not observed. Prescheduled 4 increasing doses of HDM extract could be administered in 24 of 26 patients (92.3%) except two patients who developed grade 2 SR at 15 minute after the second dose (0.2 mL) injection and grade 3 SR at 120 minute after third dose (0.3 mL) injection. SR observed within 2 hours in all three patients who experienced a SR after administration of the last dose of HDM extract.

Conclusion: UR-SCIT conducted in an outpatient clinic was safe and well-tolerated in patients with allergic rhinitis sensitized to HDM. UR-SCIT can be a safe and useful option to start a subcutaneous allergen immunotherapy for allergic rhinitis.

TP1302 | Health and satisfaction results reported by patients, after a treatment based on a modified dermatophagoides pteronyssinus extract associated with microcrystalline tyrosine (MCT)

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Background: An extract of *D. Pteronyssinus* modified with glutaraldehyde and associated with MCT has previously exhibited tolerance and effectiveness in patients with allergic rhinitis and bronchial asthma, caused by *Dermatophagoides*. The objective of this subanalysis was to assess the quality life of patients, the subjective intensity of the disease and treatment satisfaction.

Method: This trial was a prospective, observational and multi-centre study in adult patients with allergic rhinitis with or without asthma caused by *Dermatophagoides*, who received immunotherapy (*D. pteronyssinus* [DP] 100%), for 1 year. Analysed parameters included quality of life (SPRINT-15 questionnaire and AQLQ questionnaire in patients with asthma), symptom intensity, evaluated by patients (visual analogue scale, VAS) and the treatment satisfaction (TSQM questionnaire, *Treatment Satisfaction Questionnaire for Medication).*

Results: 118 patients (57% women) out of 141 recruited patients were evaluated, with an average age of 34. The following changes were observed: SPRINT-15 (global score): 2.62 (baseline) vs 1.33 (6 months) vs 1.16 (1 year) ($P < 0.0001$); AQLQ (total score): 3.03 (baseline) vs 1.23 (6 months) vs 1.45 (1 year) ($P < 0.0001$); VAS: 6.41 (baseline) vs 3.47 (6 months) vs 2.80 (1 year) ($P < 0.0001$). The global satisfaction with the treatment (TSQM) were 71.7 points at 6 months and 73.4 points at 1 year.

Conclusion: Specific immunotherapy with a house dust mite allergoid associated with MCT, in patients allergic to *Dermatophagoides*, showed improvement in health outcomes as reported by patients (Quality of Life and VAS) along with a high satisfaction with the treatment.

TP1303 | The health and economic impact of allergen therapy in patients with allergic rhinoconjunctivitis: Real-world evidence from the Czech Republic

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Background: To compare the changes in clinical outcomes and healthcare costs during the usage of subcutaneous allergen immunotherapy (AIT) in patients with allergic rhinoconjunctivitis (AR) before and after initiation of AIT in the Czech Republic.

Method: Allergen therapy data were based on prospective, non-interventional, single arm, multi-centre cohort clinical study with 2-year follow-up. Data were obtained from routinely collected medical records and only patients with two completed pollen seasons with AIT were included (n = 176). Each patient was assessed before the start of AIT and then during two consecutive years treated with subcutaneous AIT. Information about the daily occurrence, severity and symptomatic treatment used in the pollen season was obtained from patient questionnaires. In addition, demographic data and healthcare resource use and costs connected to allergic rhinoconjunctivitis were collected.

Differences between patient outcomes before and after second season with AIT therapy were tested at the 5% significance level for non-parametric Wilcoxon matched-pairs signed-ranks test. To test the differences in categorical variables, the chi-square test or Fisher's exact test was used. The costs were based on actual list prices, reimbursement tariffs and expert opinion as of 11/2018.

Results: The data showed improvement in frequency and severity of clinical symptoms reported by clinicians and patients: from 81% to 36% with persistent AR and from 93% to 28% with moderate or severe AR (both *P* -values < 0.001). The mean ARMS score (Average Rescue Medicine Score) which represents the amount of the usage of symptomatic medicine decreased from 1.9 points to 1.3 points (*P* -value < 0.001). Nevertheless, the median ARMS score did not change during treatment (2.0 points), which indicates that the greatest effect of treatment was in patients taking high number of medicines including oral corticosteroids. If the number of physician visits includes only visits that went beyond the scheduled AIT treatment, total annual healthcare costs decreased during AIT treatment by 46% (from 1282 CZK before treatment to 690 CZK after the second season with AIT).

Conclusion: AIT treatment is an effective and cost-effective treatment of AR based on medical records from the real clinical practice in the Czech Republic. However, it should be taken into the account that the environmental changes between the seasons might affect the results.

TP1304 | Allergic bronchial asthma treated with house dust mite (HDM) sublingual immunotherapy tablet (SLIT): clinical profile of patients from bengaluru allergy center, India

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Background: Allergic Bronchial asthma is mediated through type-1 immune reaction, there is also an imbalance in TH1 and TH2. Pharmacotherapy is effective in controlling the symptoms of allergic diseases, but withdrawal of it leads to reappearance of symptoms in a short span of time. SLIT corrects the TH1 and TH2 imbalance and thus effects the natural course of disease. Randomized double blind controlled studies demonstrates therapeutic efficacy of SLIT.

Method: All Clinically suspected patients underwent a questionnaire, pulmonary function test (PFT), peak expiratory flow rate (PEFR) and IgE specific enzyme immuno assay (EIA) for aeroallergens and food allergens. After subjecting to skin prick test (SPT), they were prescribed HDM SLIT tablet. On follow-up, symptom score, PEFR, medication score were noted. Statistical analysis: One way ANOVA with Dunnet's multiple comparison test.

Results: Total 165 Allergic Bronchial Asthma patients presented to our Bengaluru Allergy Centre in the year 2014 were studied. Age group ranged from 4 years to 61 years. Allergic rhinitis, urticaria, atopic dermatitis, allergic conjunctivitis, and otitis media were the multi morbidities observed. After 3 years, only about 43 patients continued to take SLIT Tablets. Among them, 7 were irregular on SLIT tablets. Symptom score reduction (based on visual analogue score from 1 to 10) ranged between 4 and 9. There was no correlation between suffering time and medication score. There were negligible adverse effects due to SLIT tablets (<1%). There was a remarkable improvement in the PEFR score (ranged from 200 to 650 lpm). There was also significant reduction in the medication score. The Line chart illustration depicts 95% confidence intervals (Dunnet) of difference between group means (medication score) over the different time periods from 2014 to 2018.

Conclusion: HDM SLIT tablet has demonstrated significant benefit by clear induction of clinical and immunological tolerance in Allergic Bronchial Asthma. It has also shown to be more patient friendly with significant lower risk profile.

TP1305 | Classification and management of gastrointestinal symptoms during omalizumab-enabled oral immunotherapy

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Background: Gastrointestinal (GI) symptoms represent a major side effect of Oral Immunotherapy (OIT) and the principal cause of its discontinuation. The safety profile of OIT can be improved with the concomitant use of omalizumab. However, GI symptoms remain frequent despite this approach, possibly owing to the rapid escalation schedule, and they are very heterogeneous in terms of presentation and severity. The aim of this study is to describe GI symptoms and their management in a large retrospective cohort of omalizumab-enabled accelerated OIT (OEAOIT)

Method: This is a monocentric, retrospective and descriptive study. Clinical charts of all patients having undergone OEAOIT at the Immunotherapy clinic of Sainte Justine Hospital (Montreal, Canada) between Dec 2016 and Dec 2018 were systematically reviewed for the occurrence of GI symptoms (nurse and MD observations, phone call report, patient diary, prescriptions and pharmacy notes). Symptoms were described in terms of date of occurrence, timing with dose ingestion, presentation as abdominal pain, reflux, vomiting or diarrhea and response to medication.

Results: During the study period, 96 patients underwent OEAOIT, to an average of 3.3 (±1.7) food allergens, and median specific IgE of 90.1 ku/L to the index food. Overall, 37 (38.5%) experienced GI symptoms. Of these, 24 (65%) had symptoms during the initial food escalation (IFE). Among these, 8 required no medical treatment and 8 received anti-H1, 4 anti-H2, and 4 received both. Twenty-six (70%) patients had GI symptoms during the up-dosing phase, 13 of which had had GI symptoms on the IFE (50%). Of these, 15 (58%) presented with transient immediate abdominal pain after dose and 11 (42%) presented with persistent symptomatology suggestive of reflux, esophagitis or gastritis, with a timing unrelated to dose ingestion. While most of the patients in the first group (14/15, 93%) resolved with anti-H2, anti-H1 or no treatment, none did in the second group. Of the latter, 7 (63.3%) responded to proton pump inhibitor (with or without dose decrease) and 4 (36.7%) patients stopped OIT (2 temporarily and 2 definitively).

Conclusion: Our results characterize two distinct phenotypes of gastrointestinal complications during OEAOIT with different management and prognosis. Despite the baseline severity of our patients and the relative frequency of GI symptoms, most were manageable with personalized treatment.

TP1306 | Grass pollen sublingual immunotherapy – experience in a UK children's hospital

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Background: In the UK, up to 10% of 6 year olds are diagnosed with Seasonal Allergic Rhinitis (SAR), with this number doubling amongst teenagers[1]. SAR not only affects the quality of life but also significantly impacts on examination performance in teenagers[2]. Desensitisation or immunotherapy involves gradually increasing exposure to the standardized grass pollen extract (Timothy grass, *Phleum pratenase*) until tolerance is achieved.

Method: This was a retrospective cross-sectional study conducted between 1st March to 30th June 2018. The first dose of sublingual immunotherapy was administered in hospital as per protocol. Questionnaires and telephone/ postal survey were used to collect data. We used the EAACI SAR scoring system, pre and post immunotherapy to assess response[3]. Our aim was to assess the impact of grass pollen sublingual immunotherapy on symptom control in children with severe SAR.

Results: 28 children undergoing sublingual pollen immunotherapy were enrolled, age range 6–17 years, median age 14 years. 64% children were monosensitised to grass/ tree pollen. 70% patients found the treatment helpful. The combined SAR score before immunotherapy ranged from 4.2-5, with median of 4.3 out of 6, implying at least moderate severity of SAR. The median score post treatment was 1.6 indicating reduction of 43%. Patients experienced symptom reduction and required lower doses and frequency of antihistamines and nasal corticosteroid sprays. Examination performance and participation in sports improved. 75% of the children with asthma reported reduced use of anti-asthma medication. 2 of the 3 patients that found the treatment unhelpful, were in their first year of treatment. This is consistent with published reports, that treatment is more effective if used for at least 18 months. The duration of treatment ranged from 7 months to complete 3 years, median duration of 22.5 months. The short duration is due to recent initiation of immunotherapy and not due to withdrawal from treatment. Patient compliance was high, only 2 patients discontinued therapy for personal reasons.

Conclusion: Sublingual grass pollen immunotherapy in SAR is effective, safe, logistically easy to administer and has a beneficial effect on co-morbid allergic disorders like asthma. Further large scale prospective studies are required to establish the above results.

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TP1307 | No correlation between conjunctival provocation test and immune globulins in a positive phase II allergen immunotherapy study with subcutaneously administered tyrosine adsorbed modified grass allergen

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Background: This Phase II study [EudraCT 2017-000333-31] evaluated the dose response relationship for a modified grass subcutaneous immunotherapy (SCIT) product with modified allergen tyrosine adsorbate (MATA) and monophosphoryl lipid A (MPL) adjuvants for allergic rhinoconjunctivitis (ARC) due to grass pollen. As a secondary endpoint immunoglobulin markers were evaluated.

Method: In total 447 patients were enrolled in this randomized, double-blind, placebo-controlled, parallel group study. Patients were randomized to one of five dose regimens of 5100, 14400, 27600 and 35600 SU and placebo. The primary endpoint was the total symptom score (TSS) as measured during a conjunctival provocation test (CPT) and was correlated to the immunoglobulins (IgE, grass-specific IgE, grass-specific IgG4 and specific IgE/total IgE ratio).

Results: A highly statistically significant dose-response ($P < 0.0001$) was shown for TSS measured during CPT for the range of cumulative doses from 5100 SU to 35600 SU. Moreover, all immunoglobulin markers showed a strong statistically significant dose-response for all cumulative doses ($P < 0.01$). However, the TSS measured during CPT did not show a relevant correlation with any of the immunoglobulin markers.

Conclusion: This study demonstrated a strong and statistically significant dose response for both TSS following CPT and Immunoglobulins separately, whilst there was no correlation between TSS and immunoglobulin values measured after CPT". These findings confirm that immunoglobulins are generally considered poor markers of efficacy.

TP1308 | Patient's characteristics safety and use of allergy immunotherapy 12 SQ HDM SLIT-tablet in real-life clinical practice in adult patients with house dust mite allergy in France – an interim analysis

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Background: House dust mite (HDM) allergy is the most common inhalant allergy, with HDM sensitisation in up to half of the patients with a clinical diagnosis of allergic rhinitis (AR) in Western Europe. The 12 SQ HDM SLIT-tablet is a sublingual form of allergy immunotherapy (AIT) indicated for HDM respiratory allergy in adults and adolescents. The aim of this study was to describe the profile of patients enrolled, the safety and tolerability after first administration of the SQ HDM SLIT-tablet.

Method: The CARIOCA study is a non-interventional, multicenter, longitudinal, prospective study. Inclusion criteria were adults sensitized to HDM with persistent moderate-to-severe HDM AR despite the use of symptom-relieving medication, and/or HDM allergic asthma not well controlled by inhaled corticosteroids and associated with mild-to-severe HDM AR. Data were collected via an eCRF and a patient questionnaire (AQ). A specific AQ were filled by patient if sleep disorders related to HDM allergy were mentioned in the eCRF. This interim analysis shows the first 6 months of the inclusion period.

Results: From May to November 2018, 798 patients were included: mean age (SD) 34 (±11) years; 58% female, 65% polysensitised; 11 patients were under concomitant AIT (9/pollen and 2/hair dander). SQ HDM SLIT-tablet was prescribed for AR in 77%, for asthma in 3% and for both in 20% of patients. Considering clinical manifestations 34% had asthma and 89% a moderate-to-severe rhinitis (ARIA). Asthma was well controlled in 54%, partly controlled in 29% and uncontrolled in 17%. Sleep disorders were reported by 39% of patients with AR and 41% of patients with asthma.

Overall, 18% of the patients reported at least one adverse event (AE) after the first intake. Most frequent AEs were throat irritation (40%), oral pruritus (37%) and ear pruritus (21%). Due to AEs after the first intake, 4 patients (0.5%) discontinued treatment. There was no systemic allergic reaction.

Conclusion: In real life, patients receiving the SQ HDM-SLIT tablet are mostly polysensitised and one third had concomitant asthma, partly or uncontrolled in half of the cases. Treatment was well tolerated and no new AE were identified according to the summary of product characteristics.

TP1309 | Real-life adherence of subcutaneous (SCIT) and sublingual (SLIT) AIT: A retrospective, long-term cohort analysis in Germany

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Background: Data on real-life outcomes SCIT are scarce. To evaluate the real-life adherence to SCIT and SLIT vaccines within the prescribing guidelines, we analyzed data on AIT prescriptions of patients allergic to grass, tree pollen or house dust mites (HDM).

Method: The analyses were conducted with IMS LRx® (IQVIA, Frankfurt, Germany) a database which covers approx. 60% of all German statutory prescriptions. We compared the adherence of cases (n = 159.685) with an initial AIT prescription in 10/2009-9/2013 (grass), 6/2010-5/2013 (tree) or 2/2010-1/2014 (mites). We analyzed 4 subcutaneous grass AIT products and 2 grass tablets, 4 subcutaneous and 2 sublingual trees products, and 4 different subcutaneous HDM products. The analyses were descriptive and consisted of the following two outcomes: shares of patients with adherence of ≤ 1 year, ≤2 years, ≤3 years and > 3 years and days on therapy with the respective preparations.

Results: 59.6-63.8% (dependent on product) of patients receiving grass SCIT reached the third treatment year, whereas adherence in patients treated with grass tablets was 29.5/33.7% (dependent on product). For tree pollen treatment adherence was 56.7-62.3% for SCIT and 29.4/36.8% for SLIT. In subcutaneous HDM AIT adherence in the third year was 60.7-64.5%. The day-on-therapy analyses of grass AIT patients revealed the highest number of days on therapy for Allergovit® (1,034 days in mean) and the lowest for grass tablets (488 and 462 days in mean). For tree pollen AIT, the results for days on therapy were rather close to those in the grass pollen AIT patients. In HDM AIT, patients treated with Acaroid® showed the highest number of mean treatment days (1,040 days), which was close to the recommended three years. Irrespective of the allergen, the adherence in children (5-11 years) was the highest compared to adolescents (12-17 years) and adults (18-50 years).

Conclusion: According to the recent guidelines a minimum of 3 years of AIT is recommended to achieve long-term efficacy. In addition, poor adherence is a contraindication for AIT. This real-life analysis of prescription data in allergic patients revealed considerable differences in adherence between subcutaneous and sublingual AIT products in favor to the subcutaneous application form and underlines the importance of strategies to improve therapy adherence.

TP1310 | Impact of subcutaneous house dust mite (HDM) allergoid AIT on HDM-triggered allergic rhinitis and/or asthma: A retrospective real-life, long-term cohort analysis in Germany

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Background: Data on real-life outcomes of subcutaneous immunotherapy (SCIT) are scarce. To evaluate the long-term effectiveness of subcutaneous AIT (SCIT) with a HDM-allergoid preparation in the treatment of HDM-triggered allergic rhinitis or asthma, we analyzed data on medical prescriptions of symptomatic medication in the relevant patient population.

Method: The analyses were conducted with IMS LRx® (IQVIA, Frankfurt, Germany) a database which covers approx. 60% of all German statutory prescriptions. We compared two groups of HDM allergic patients: one group treated for at least 2 years with Acaroid® (n = 2,350), the control group received symptomatic medication only (n = 64,740). We analyzed data from January 2008 until February 2017 (when nasal corticosteroids (NCS) became no longer prescription bound in March 2017). The impact of SCIT was assessed by comparing the number of symptomatic prescriptions for allergic rhinitis or asthma between the SCIT group and the control group. The analysis was structured as a comparison between a pre-index period (at least 18 months before SCIT) and a follow up period (covering at least 2 years following SCIT) with a time adjustment for the latter period. The onset of asthma was assessed as probability of developing asthma after start of SCIT in the subpopulation of patients not yet suffering from asthma.

Results: 37% of Acaroid® treated patients required asthma medication before starting SCIT. 30.4% of Acaroid® patients were 5-12 years old. Considering the symptoms of allergic rhinitis, the SCIT group had 59.7% less prescriptions of symptomatic medication in the follow up period compared to control group ($P < 0.0001$). The number of asthma medication prescriptions was 10.8% lower in the SCIT group than in the control group ($P = 0.0145$). In children, the number of asthma prescriptions was 39.1% lower compared to the control group ($P < 0.0001$). Looking at the individuals not taking any asthma medication in the pre-index period, the probability for asthma development in the SCIT group was significantly lower (OR = 0.812, $P = 0.008$) than in control group.

Conclusion: This real-world analysis of prescription data in patients suffering from house dust mite allergy shows that SCIT with the HDM allergoid preparation reduced number of prescriptions of symptomatic allergic rhinitis and asthma medication, decelerated allergic rhinitis progression and reduced the probability of asthma development compared to control patients.

TP1311 | SQ house dust mite sublingual immunotherapy-tablet demonstrated clinically relevant efficacy in Japanese children with allergic rhinitis

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Background: The SQ house dust mite (HDM) sublingual immunotherapy (SLIT) tablet (Torii, Japan/ALK, Denmark) treatment has been shown to be effective against HDM allergic rhinitis (AR) in Japanese children (5-17 years) with moderate-to-severe HDM AR and has been approved for the pediatric HDM AR indication from February 2018 in Japan. This abstract reports patients' satisfaction to treatment during the Phase III trial (JapicCTI-152953).

Method: In this randomized, double-blind, placebo-controlled trial, 458 Japanese children were randomly assigned to a daily SQ HDM SLIT-tablet (10,000 JAU) or placebo (1:1) treatment for 1 year. Four endpoints were evaluated as follows, the change over time in adjusted mean total combined rhinitis score (TCRS) comprising AR daily symptom score (DSS) and AR daily medication score (DMS) during the treatment period, the percentage of AR symptom-free days (the rate of days when the AR DSS and AR DMS are 0 during the evaluation period, *post-hoc* analysis), quality of life using Japanese Allergic Rhinitis Standard Quality of Life Questionnaire (JRQLQ) No.1, and a global evaluation by physicians and subjects (Much better, Better, The same, Worse, Much worse).

Results: The adjusted mean TCRS declined during the treatment period. A significant reduction in TCRS in the 10,000 JAU group was noted from Week 4-6 compared with that in the placebo group (Placebo 7.74, 10,000 JAU 7.25, $P = 0.0238$), and in all subsequent evaluation periods. The percentage of AR symptom-free days increased over time and showed statistical significance compared to placebo at Week 44-52 (Placebo: 5.4, 10,000 JAU: 10.2, $P = 0.013$). The JRQLQ (see table), and global evaluation by physicians and subjects, were significantly improved compared to placebo at week 52 ($P < 0.0001$, respectively).

Conclusion: Treatment with SQ HDM SLIT-tablet significantly improved symptoms from 4 to 6 weeks after start of treatment, and improves quality of life and patient satisfaction in Japanese children with allergic rhinitis.

JRQLQ general state	0: "Fine"	1	2	3	4: "Crying"
SQ HDM SLIT 10 000 JAU (n = 209)	13.9%	45.0%	30.1%	9.1%	1.9%
Placebo (n = 217)	7.8%	37.8%	33.2%	20.3%	0.9%

TP1312 | Oral and sublingual immunotherapy: A systematic review of clinicaltrials.Gov records

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Background: Clinical trials are the best way to appraise the effectiveness of individual pharmacological and non-pharmacological interventions; systematic reviews and meta-analysis of those trials are necessary for physicians to deliver interventions supported by the best available evidence. Data concerning trials involving oral and sublingual immunotherapy registered at ClinicalTrials.gov are systematically reviewed as a whole in this submission.

Method: ClinicalTrials.gov records matching the queries "oral immunotherapy" and "sublingual immunotherapy" were included (search date: December 3, 2018). Only interventional studies in patients with rhinitis, asthma, and food allergies were considered. Compatible records were expressed into numerical, dichotomous, and categorical variables.

Results: 265 ClinicalTrials.gov records were collected; 87 of these registries were excluded because of: (i) recruitment of patients with non-allergic diseases (n = 72); (ii) observational design (n = 15). A total of 178 records with oral (n = 82) and sublingual (n = 96) immunotherapy in allergic diseases were analysed. Results are shown in Table 1.

Conclusion: The evidence of medical interventions collected over clinical trial records is a novel approach to translate scientific data into clinical practice guidelines as a mean to guide decisions by physicians and healthcare policymakers. Disclosure of allergy trial results is a pragmatic way to lead decision-making about healthcare systems; improving the overall processes of patient informed consent.

	Oral immunotherapy (n = 82)	Sublingual immunotherapy (n = 96)
Conditions		
Food allergy	69 (99 ± 19)	13 (35 ± 5)
Allergic rhinitis	12 (57 ± 13)	59 (270 ± 36)
Asthma	1 (51)	9 (170 ± 56)
Asthma plus allergic rhinitis	—	11 (107 ± 50)
Atopic dermatitis	—	2 (167 ± 73)
Healthy	—	2 (48 ± 18)
Clinical trial phase		
I	9 (31 ± 4)	19 (51 ± 6)
II	36 (55 ± 7)	21 (165 ± 16)
III	10 (358 ± 102)	34 (402 ± 53)
IV	5 (64 ± 16)	14 (68 ± 8)
Not applicable	22 (66 ± 11)	8 (56 ± 16)
Status		
Completed	42 (76 ± 17)	75 (224 ± 30)
Not completed(*)	40 (187 ± 30)	21 (150 ± 33)

TP1313 | Safety of subcutaneous immunotherapy in patients with asthma- reduced FEV1 as a predictor of systemic adverse events

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Background: Allergen immunotherapy (AIT) is an established method of treatment of allergic diseases and its efficacy and safety has been proved in countless studies. Current EAACI guidelines recommend AIT as safe in patients with controlled mild-to-moderate asthma, but the European Survey on Adverse Systemic Reactions in Allergen Immunotherapy identified the diagnosis of asthma as one of the major risk factors for systemic reactions. The aim of this study was to assess the safety of subcutaneous allergen immunotherapy (SCIT) in patients with mild-to-moderate, controlled asthma and assess the risk factors of local and systemic side effects (SE) in that population, compared to patients without asthma.

Method: We monitored subcutaneous immunotherapy in 948 patients with allergic rhinitis (AR) treated over the course of 2 years. 457 patients had a concomitant diagnosis of asthma and 491 were treated for AR only. We performed lung function tests in all patients before initiating AIT and recorded all spirometric data, along with medical history and detailed information for each SCIT administration. We compiled all data in a comprehensive database and analyzed it.

Results: Out of 948 patients, 147 (15.5%l) experienced at least one episode of systemic adverse events (AE) and 399 (42%) observed local reactions. We did not observe a significant difference in the occurrence of adverse reactions between asthmatics and the control group (46.2% vs 38.3% for local and 16.2% vs 14.9% for systemic SE, respectively; $P > 0.05$). Either univariate, nor multiple logistic regression did not point to asthma as a risk factor of adverse events in our study group. However, further analysis revealed that asthmatics with reduced FEV1 (below 80% of predicted), as measured before initiating AIT, were at an increased risk of experiencing systemic events (OR = 1.7, $P < 0.05$). Moreover, this was the only subgroup in which we observed a noticeably lower incidence of systemic AEs with allergoid preparations, compared with natural allergen extracts (15.4% vs 38%, respectively, compared to 15.8% vs 14.0% in patients with FEV > 80% predicted)

Conclusion: Subcutaneous allergen immunotherapy is safe and well tolerated in asthmatic patients. While the diagnosis of asthma itself does not appear to be a risk factor of adverse events, patients with reduced initial FEV1 values experience systemic side effects more frequently. Moreover, that subgroup seems to benefit more from allergoids' improved safety profile, compared to non-asthmatics.

TP1314 | Post-marketing survey on the safety and efficacy of the sq house dust mite (HDM) sublingual immunotherapy-tablet in Japanese patients with hdm-induced allergic rhinitis (interim analysis 2016-2018)

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Background: The SQ house dust mite (HDM) sublingual immunotherapy (SLIT) tablet (MITICURE, Torii, Japan/ALK, Denmark) has been available since December, 2015 in Japan, and approved for the pediatric HDM allergic rhinitis (AR) indication in February, 2018. Post-marketing surveillance of the SQ HDM SLIT-tablet has been conducted to investigate the safety and efficacy of long-term administration (3 years) in HDM-induced AR patients.

Method: The evaluations of safety and efficacy are planned to conducted at 6-, 12-, 24- and 36-months after treatment initiation for all registered patients. The main outcomes of interest were patient demography, adverse drug reactions (ADRs), laboratory measurements, nasal symptoms, quality of life using Japanese Allergic Rhinitis Standard Quality of Life Questionnaire (JRQLQ) No.1, and an global evaluation (Much better, Better, The same, Worse, Much worse). This interim analysis evaluated patients from July 2016 to September 2018.

Results: 519 patients (mean age 27.2 years, male 57%) were included for safety analysis, of whom about 50% were < 20 years of age (31.7% < 15 years, and 15.4% 15-19 years). No deaths or episodes of anaphylactic shock were reported in this period. 116 ADRs were reported in 82 (15.8%) patients. Most ADRs were mild local reactions, such as oral pruritus and mouth swelling at the site of administration. 93 events occurred within one month of treatment initiation, of which 41 events occurred within the first week. 495 patients were included for efficacy analysis. The JRQLQ and global evaluation showed an improvement from baseline, and approximately 80% of patients were "satisfied" after one year of treatment.

Conclusion: An interim analysis of a post-marketing surveillance study does not identify new safety concerns. In a real life setting in Japan, SQ HDM SLIT-tablet, improves quality of life and overall symptoms during the first year of follow-up.

TP1315 | Monitoring immune response and patient attitudes during sublingual immunotherapy in patients with respiratory allergic disease (RAD)

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Background: A machine-learning algorithm reliably differentiates between patients receiving active treatment with sublingual immunotherapy (SLIT)-tablet versus placebo in clinical trials, using baseline and follow-up measurements of allergen specific IgE and IgG_4. The algorithm outputs an antibody responder test (ART) score (range 0 to 10, scores > 5, = 5 and < 5 indicate positive, inconclusive and negative immunological response to treatment, respectively).

Method: Patients aged 18-65 years with allergic rhinitis with or without concomitant asthma, sensitisation to grass pollen (skin prick test wheal > 3 mm and specific IgE ≥ class 2), and a relevant history of allergy symptoms despite treatment with antihistamines and/or nasal steroids were included in this single-arm study of treatment with grass SLIT tablet. Patients were excluded if they had other significant allergies or uncontrolled asthma. Patients were evaluated at baseline, 8-weeks, 14-weeks (peak season), and 32-weeks (post-season) of treatment. Evaluations included a symptoms and medication assessment, spirometry, immunological and serological measurements, exhaled nitric oxide (FeNO), calculation of the ART score, and a qualitative assessment of the patients' understanding and reaction to the ART score.

Results: A total of N = 20 patients (9 male, age 36 ± 11 years, grass pollen sIgE 20.3 kU_A/L (1.8->100 kU_A/L) and $sIgG_4$ 0.2 mg_A/L (0.06-1.08 mg_A/L) at baseline) were included in the study. 14 patients also demonstrated positive skin prick test to allergens other than Timothy grass (Birch = 6, mugwort = 3, horse = 3, dog = 1, cat = 6, mold = 4, house dust mite = 2). One patient was lost to follow-up after visit 2, and one patient did not complete assessment with the ART score. All patients completing the ART score calculation had values corresponding to a positive immunological response to treatment. Most patients (14/18) had a maximum ART score of 10 at all three follow up visits. In answer to the questions: "What are the results of the test?" and "What do the results mean to you?", patients expressed positive, optimistic or motivational attitudes to their treatment (15/18), reassurance (13/18), or mechanistic understanding of how the treatment worked (12/18).

Conclusion: The ART score was associated with a positive, optimistic or motivational attitude to treatment by the majority of patients. Further studies are required to evaluate the impact of the use of the tool on improving patient adherence.

TP1316 | Is it possible to improve the efficiency of allergen-specific immunotherapy in children with seasonal allergic rhinoconjunctivitis?

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Background: It is well known that the effectiveness of allergen-specific immunotherapy (AIT) is higher in patients with seasonal allergic rhinoconjunctivitis (AR) than in patients with other allergic diseases. At the same time, there are cases of both low efficacy and a complete lack of treatment result, which is most often associated with the wrong choice of the relevant allergen due to the presence of cross-allergy in pollen sensitization. In this regard, component-resolved diagnosis (CD) can help determine the objective criteria for the prescription of AIT.

Method: The study included 20 children with AR aged from 7 to 14 years who experienced worsening course of the disease during sublingual AIT (SLIT) with birch pollen allergens. All patients have undergone: prick test with birch and timothy allergens, the determination of specific IgE for birch and timothy allergens, as well as for their major (rBetv1, rPhlp1,5) and minor components (rBetv2,4, rPhlp7,12) by ImmunoCAP, Phadia AB, Sweden.

Results: According to generally accepted results of the survey, 14 patients were sensitized to birch and timothy, 6 - only to birch. According to the results of the CD, 12 patients were diagnosed with true sensitization to timothy (rPhlp1,5), of whom 4 patients also had minor allergens (rBetv2, rPhlp7,12). A major allergen was detected in 3 patients - rBetv1 in combination with birch minor allergens rBetv2, 4, as well as minor herb allergens rPhlp 7, 12. At the meantime, 5 patients had only minor birch allergens (rBetv2,4). Clinical manifestations during the flowering period of trees may be associated with cross-properties of the detected minor allergens. According to the results of the CD, 8 patients were recommended the SLIT with timothy. A year later high efficiency of the treatment was marked among all the patients.

Conclusion: Thus, the component-resolved diagnosis can help to choose the relevant allergen and thereby ensure high efficacy of the allergen-specific immunotherapy.

TP1317 | Rapid dose escalation with monomeric tree pollen allergoid drops is well tolerated in patients with allergic rhinoconjunctivitis and point towards clinical effects

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Background: Carbamylated monomeric allergoids play a special role in the treatment of pollen allergies for their lower allergenic potential and susceptibility to enzymatic degradation. So far, birch pollen sublingual allergoids are marketed with doses up to 1,000 UA daily. Aim of this investigation was to identify a safe dose range for once-daily administration up to 50,000 UA of sublingual drops in patients with allergic rhinoconjunctivitis.

Method: A randomized, double-blind, placebo-controlled trial was conducted with 21 patients in 5 centres in Germany. Updosing was performed before the birch pollen season 2018 in 3 visits within 8 days. Doses increased from 2,000 UA to 50, 000 UA in 5 steps. The individual maximum tolerated daily dose was maintained for another 62 days. Safety and clinical tolerability were assessed by means of solicited (local/systemic) and unsolicited adverse drug reactions (ADRs), physical examination, vital signs and routine laboratory tests. The clinical impact was analysed by conjunctival allergen provocation testing and immunological status at screening and last visit.

Results: Overall, no fatality, no serious nor severe ADRs occurred during the trial. No epinephrine was used. The intended cumulative dose of 3,302,00 UA ± 30% was received by more than 85% of the actively treated patients. During treatment, 1 patient experienced grade I-systemic allergic ADRs (mild rhinitis) and was withdrawn from the trial. No systemic ADR grade II or higher occurred. Solicited and unsolicited local ADRs occurred in 1.1% of all doses and only during updosing. Their severity was mild and no dose adjustment was necessary. One patient discontinued the trial because of unrelated worsening of seasonal allergic symptoms.

In the placebo group, the reactivity of conjunctival mucosa was only slightly reduced (-7.5%) from screening visit to last visit. In contrast, reactivity decreased significantly by 19.5% (P = 0.038) in actively treated patients. During treatment, birch pollen specific IgG4 increased 1.4-fold (P = 0.173) in the placebo group and 1.7-fold (P = 0.061) in the actively treated group, close to a statistically significant difference. Specific IgE significantly increased only in actively treated patients (1.7-fold, P = 0.001).

Conclusion: This early phase clinical dose escalation study has successfully demonstrated the safety and the feasibility of this high dose concept of sublingual allergen immunotherapy with the carbamylated allergoid.

TP1319 | Strong dose-response on immunoglobulin markers during a phase II allergen immunotherapy study with subcutaneously administered tyrosine adsorbed modified grass allergen + MPL

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Background: The results of this Phase II study [EudraCT 2017-000333-31] evaluated the dose response relationship for a modified grass allergen subcutaneous immunotherapy (SCIT) product (1.0 mL) with modified allergen tyrosine adsorbate (MATA) and monophosphoryl lipid A (MPL) adjuvants for the treatment of allergic rhinoconjunctivitis (ARC) due to grass pollen.

Method: In total 447 patients with grass pollen-induced ARC were enrolled in this randomized, double-blind, placebo-controlled, parallel group study. Patients were randomized to one of five dose regimens of 5100, 14400, 27600 and 35600 SU and placebo. As a secondary endpoint the immunoglobulin markers (total IgE, grass-specific IgE, grass-specific IgG4 and specific IgE/total IgE ratio) were evaluated.

Results: For all immunoglobulin markers a strong statistically significant dose-response was shown for a wide range of cumulative doses from 5100 SU to 35600 SU. Grass-specific IgE, grass-specific IgG4 and specific IgE/total IgE ratio demonstrated statistically significant increases compared to placebo for all cumulative doses (P < 0.01), including the currently marketed dose of 5100 SU in Europe.

Conclusion: An ultra-short course of 6 injections with allergoid grass SCIT treatment with adjuvants MATA and MPL is associated with significant increases in immunoglobulin markers for a wide range of cumulative dose levels indicating a strong therapeutic response.

TP1320 | Results of scit with a polymerised extract, associated with microcrystalline tyrosine, in allergic patients to dermatophagoides Spp. According to their sensitization profile to Der p1 and Der p2

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Background: The use of molecular diagnosis of allergic patients could be helpful to determine the most appropriate immunotherapy treatment. However, there are few studies which evaluate the relationship between molecular diagnosis and the safety or efficacy of treatment. The objective of this study was to establish the clinical response of a group of patients allergic to *Dermatophagoides pteronyssinus*. and treated with a polymerised extract associated with microcrystalline tyrosine (MCT), according to their sensitization profile to Der p1 and Der p2.

Method: The trial was a prospective, observational and multi-center study in patients with allergic rhinitis caused by the house dust mite *Dermatophagoides*, who received immunotherapy (*D. pteronyssinus* [DP] 100%), for 1 year. Patients were classified into three groups, according to the amount of specific IgE (class): "predominant sensitisation (PS) to Der p1" (Der p1 > Der p2), "PS to Der p2" (Der p1

Results: Molecular diagnosis was obtained from 99 patients (83.9%) out of 118 evaluated patients. 12% did not show predominant sensitisation to Der p1 or Der p2. 5% had only sensitisation to Der p 1 and 12% to Der p 2. Patient distribution according to their sensitized profile was: PS Der p 1: 11.1%; PS Der p 2: 37.4% and No PS: 51.5%. There were no significant changes between the 3 groups, in any of the analysed variables (baseline vs 1 year).

Conclusion: Specific immunotherapy with an allergoid of *D. Pteronyssinus* associated with MCT shows good clinical results in allergic patients to *Dermatophagoides*, independently of their sensitization profile to Der p 1 and Der p 2.

TP1321 | Trial design for safety evaluation of an accelerated dose escalation schedule with one strength of a 6-grasses pollen allergoid in children and adolescents

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Background: Subcutaneous specific immunotherapy (SCIT) with a hypoallergenic grass pollen allergoid is an effective and tolerable treatment method. Recently we have shown that accelerated dose escalation is safe and well tolerated in adults with grass pollen related AR and/or asthma. This study investigates the safety and tolerability of an accelerated dose escalation scheme with only one strength of the preparation in children and adolescents.

Method: 18 sites in Germany, Poland, Spain and Russia will recruit patients (5 to < 17 years) with a positive skin prick test to grass pollen allergens, specific IgE [>0.70 kU/L] and symptoms of rhinoconjunctivitis on grass pollen exposure documented in the medical history. The safety and tolerability of an accelerated dose escalation scheme (3 injections with strength B) will be compared with the standard escalation scheme (7 injections with strength A+B) of a hypoallergenic grass pollen in a multicentre phase II clinical trial. Both groups will receive 2 additional maintenance doses. All adverse events will be recorded. Patients and investigators will assess the tolerability of the therapy using a 5-point Likert scale.

Results: The study design has been approved by Competent Authorities and Ethic Committees in all participating countries. Approximately 200 male and female outpatients, aged 5 to < 17 years, will be screened. It is planned to randomize 140 patients, 35 patients in each active treatment group. The use of an alternative dose escalation schemes with less injections is common in daily practice. The current trial investigates a treatment scheme with 3 dosing escalation steps with one strength in a controlled environment. As recently shown in adult patients, we expect these as the minimal number of injections for a dose escalation of an allergen immunotherapy with the 6-grasses pollen allergoid in children and adolescents, too.

Conclusion: The advantage of this new one strength high-dose allergen immunotherapy (AIT) option is that administration of less injections is comfortable especially in children and minimizes the risk to confuse vial A with vial B. For the patients it is convenient to get less injections and to have less doctor's visits.

TP1322 | A retrospective study on the effects of subcutaneous immunotherapy using house dust mites in pediatric patients with allergic rhinitis

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Background: The prevalence of allergic rhinitis (AR) caused by house dust mite (HDM) has increased. In addition, AR due to pollinosis and pollen-food allergy syndrome (PFAS) followed by pollinosis has emerged in our area. In this study, we aimed to investigate the effect of subcutaneous immunotherapy (SCIT) using HDM for AR and associated allergic diseases in pediatric patients.

Method: We retrospectively analyzed 130 pediatric patients with AR and associated allergic diseases who received SCIT using HDM at our hospital.

Results: The average age of patients was 8.7 years; further, 45 patients had asthma, 25 patients had pollinosis, and 18 patients had PFAS before treatment with SCIT using HDM. All patients regularly used antihistamine and local steroids. Of these, 127 (96.6%) patients used these drugs only as required within 6 months after receiving SCIT using HDM.

There were 14 (0.04%) reported cases of systemic adverse reactions for a total of 3356 injections. Moreover, 9 patients experienced

anaphylaxis, and 5 patients experienced systemic urticaria. The most common cause of anaphylaxis was no premedication.

Further, 8 of 29 (27.5%) patients developed pollen sensitization in the after 2-year SCIT group, and 22 of 42 (53.6%) patients developed pollen sensitization in the after 3-year SCIT group. In addition, 17 (94.4%) of 18 patients reported transient tolerance to PFAS symptoms. Only 1 patient developed new-onset asthma, but no patient developed PFAS. Only few patients reported less aggravation of atopic dermatitis in winter, whereas other patients did not express the positive effects of SCIT using HDM for any associated allergic diseases.

Conclusion: Allergen immunotherapy is currently the only disease-modifying treatment method that is very effective for the treatment of AR and associated allergic diseases. However, we still cannot reduce the risk of new allergic sensitization. Therefore, further studies need to be conducted to assess the effects of SCIT using HDM on AR and associated allergic diseases.

TP1323 | Early efficacy of HDM allergen immunotherapy in patients with allergic rhinitis

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Background: Allergic rhinitis (AR) is the most common atopic disease, and allergen immunotherapy (AIT) is the only effective treatment that can change the course of AR. This study aimed to evaluate the early efficacy of HDM-AIT in AR.

Method: This was a prospective study enrolling 70 patients received subcutaneous immunotherapy. Visual analogue scale (VAS) and rhinoconjunctivitis quality of life questionnaire (RQLQ), serum specific IgG4 (sIgG4), basophil activation test (BAT) and skin prick test (SPT, only followed up at V0 and V2) were serially followed up at baseline (V0), the completion of initial treatment (V1) and the first-stage of maintenance treatment (V2).

Results: 24 patients were lost during followup, corresponding to the dropout rate of 34.29%. Compared with V0, the VAS and RQLQ assessed at V1 and V2 were significantly decreased (presented as median with the order of V0-V1-V2, similarly hereinafter, VAS: 23.00-11.50-13.00, RQLQ: 49.00-32.00-31.00) ($P < 0.001$). The median score in specific VAS and RQLQ were as followed: sneeze (5.00-3.00-3.00), rhinorrhoea (6.00-3.00-3.00), rhinocleisis (4.00-2.50-3.00), rhinocnesmus (5.00-2.50-2.00), eye symptom (2.00-1.00-2.00), and activity (6.00-3.00-4.00), sleep (4.50-3.00-3.00), general problems (10.50-7.50-5.00), practical problems (7.00-5.00-5.00), nasal symptoms (8.50-6.00-6.00), ocular symptoms (3.50-1.00-2.00), emotions (6.00-3.50-4.50). The median levels of sIgG4 to Der p were significantly higher than those in the previous stage (13.05-36.84-62.34, mgA/L) ($P < 0.001$). However, no noticeable difference was found in the response of SPT or BAT during followup.

Conclusion: HDM-AIT could significantly alleviate the symptoms of patients with AR, improve the quality of life, and induce the production of protective antibody sIgG4. However, it had no effect on the skin reaction or the activity of basophils in peripheral blood.

TP1324 | Allergen immunotherapy (AIT) with both perennial allergens show better control of AR than regular pharmacotherapy and AIT with HDMs is more effective than parietaria in the treatment of asthma

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Background: Little is known on the comparison among the degree of symptom control in allergic rhinitis (AR) with/without asthma patients treated with subcutaneous immunotherapy (SCIT) and those on pharmacotherapy. Aim: An observational study was performed evaluating the level of symptom control, Quality of life (QoL), present medication use, asthma control test (ACT), Forced expiratory volume in one second (FEV1) % at 3 years after starting either pharmacotherapy or SCIT for patients with AR due to Parietaria pollen and house dust mites (HDMs) allergen.

Method: A total number of 250 *Patients registered in our allergy outpatient clinic* diagnosed with AR with/without asthma between 2013 -2016 were included. Among these patients, 150 had been started on SCIT at the time of their initial visit, and 100 were prescribed guideline-based pharmacotherapy

In 2017, patients current the level of *t*otal symptom scores, Visual analogue scale (VAS) symptom scores, VAS - QoL scores, VAS satisfaction scores, Medication scores, RhinAsthma Patient Perspective score, medication use score and ACT score and $FEV_{1\%}$ were assessed compared for pre- and after treatment between the patients.

Results: 72% of the patients completed the study. [120 (%80) patients immunotherapy, 60 (%60) patients pharmacotherapy group]

At 3 years after the beginning of treatment, in both immunotherapy groups total rhinitis symptom scores, VAS scores, VAS -QoL scores, VAS satisfaction scores, Medication scores, RhinAsthma Patient Perspective scores showed lower degree than the pharmacotherapy group. The FEV1% at baseline was not statistic significantly increased than before in both immunotherapy groups.

While total asthma score and ACT score were significantly improved than baseline in HDMs immunotherapy group they didn't change in parietaria pollen immunotherapy group.

85% of HDMs immunotherapy patients and 70% parietaria HDMs immunotherapy patients didn't use any medical treatment for AR anymore, whereas pharmacotherapy patients were still on medical treatment.

Conclusion: This observational real life study suggest that both HDMs and parietaria pollen SCIT have good effect on AR. Although both *SCIT* demonstrate to be effective on AR, the results of this study suggest that the efficacy of HDMs SCIT on asthma may be better than parietaria pollen SCIT.

TP1326 | Shortened updosing with subcutaneous allergy immunotherapy: Results from a safety and tolerability trial

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Background: Alutard SQ is a widely used subcutaneous allergy immunotherapy product typically updosed by 11 or more injections. To offer patients the benefit of fewer visits to the physician, this clinical trial was conducted to evaluate the safety and tolerability of shortened updosing schedules.

Method: This partly randomised, parallel group, controlled, open label, multinational trial was conducted in adolescents and adults (12-65 years) with moderate-severe allergic rhinoconjunctivitis (EudraCT 2017-000971-97). Subjects were treated with Alutard SQ grasses and rye ('grass'), Alutard SQ birch ('tree') or Alutard SQ house dust mites ('HDM'). 4 treatment schedules were applied: subjects receiving grass treatment were randomised to updosing by 11 or 7 injections (grass-11 and grass-7) and subjects receiving birch or HDM treatment were updosed by 7 injections (tree-7 and HDM-7). The primary endpoint was the number of treatment-related adverse events (AEs).

Results: 340 subjects were treated (grass-11: 85, grass-7: 85, tree-7: 87, HDM-7: 83). 89 (26%) were adolescents (12-17 years).

No major differences in the proportion of subjects who experienced treatment-related AEs were observed (grass-11: 76%, grass-7: 80%, tree-7: 76%, HDM-7: 84%). More treatment-related AEs occurred in the grass-11 group than in the grass-7, tree-7 and HDM-7 groups (grass-11: 711, grass-7: 561, tree-7: 444, HDM-7: 446). Most treatment-related AEs were mild (90%) or moderate (9%) reactions related to the subcutaneous administration.

Severe treatment-related AEs mainly occurred in the grass groups (grass-11: 8% of subjects, grass-7: 7%, tree-7: 0%, HDM-7: 1%) and most subjects discontinued due to treatment-related AEs in the grass-7 group (grass-11: 1%, grass-7: 8%, tree-7: 0%, HDM-7: 4%).

5 subjects experienced serious treatment-related AEs: 4 in the grass-11 group (anaphylactic shock, 2x anaphylactic reaction, hypersensitivity) and 1 in the grass-7 group (hypersensitivity). No deaths occurred.

There were no major differences in local administration site reactions (grass-11: 74% of subjects, grass-7: 78%, tree-7: 74%, HDM-7: 82%), vital signs, PEF or physical examinations.

There were no indications that the safety and tolerability profile differs between adolescents and adults (treatment-related AEs: adolescents: 71-86%, adults: 73-85%).

Conclusion: 7 injections updosing schedules with Alutard SQ products with grass, tree or HDM have an acceptable safety and tolerability profile for adolescents and adults (12-65 years).

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TP1327 | Pilot study to determine effect of feeding cat food made with egg product containing Anti- Fel D1 antibodies to cats on human allergy symptoms

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Background: Fel d1 is the primary allergen with 90% of cat-allergic individuals reacting to this allergen. Previous research in our laboratory showed that feeding cats a diet containing chicken egg product with anti-Fel d1 IgY antibodies (IgY) decreases active Fel d1 on cats. The objective of this controlled, double-blinded pilot study was to evaluate the effect of feeding cat food made with chicken eggs containing IgY on subsequent human exposure in cat-allergic individuals.

Method: Study protocol was reviewed and approved by Washington University School of Medicine IRB Committee. Clear plastic environmental chambers were set up indoors within the research center. Blankets on which cats had laid and shed hair were placed into the chambers as the source of Fel d1, and a fan circulated air within the chambers for 36 hours to "load" the environment prior to initiating testing. Environmental allergen load was sampled using petri dishes within each chamber. Fifteen adult human subjects with known allergies to cats (subjects with asthma were excluded), and who had previously responded variably to high vs low levels of Fel d1 completed quality of life questionnaires (Throat Nose Symptom Scores [TNSS] and Total Ocular Symptom Score [TOSS]) every 15 minutes while spending 3 hours within the chamber. Each subject had three exposures: 'Priming exposure' during week 1 in chambers loaded with cat hair from cats fed 'control' diet; and during week 2 and 4 when they were exposed to either hair from cats fed 'control' diet or 'test' diet. Subjects served as their own controls in the analysis, reducing subject-to-subject variability.

Results: Feeding cats the cat food made with chicken eggs containing anti-Fel d1 IgY resulted in less Fel d1 in the environmental chambers. There was considerable variability in participant responses but TNNS were numerically lower, with a significant reduction in runny noses ($P < 0.05$) in subjects in chambers loaded with cat hair from cats fed 'test' diet. TOSS correlated with environmental Fel d1.

Conclusion: Despite strong variability, the reduction in TNSS and TOSS scores suggest a benefit from feeding cats food made with chicken eggs containing anti-Fel d1 IgY and supports the need for further study.

TP1328 | Feeding Anti-Fel d1 chicken antibodies decreases active Fel d1 on cat hair

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Background: Fel d1 is the primary allergen with 90% of cat-allergic individuals reacting to this allergen. Fel d1 produced in the salivary glands is distributed to the haircoat during grooming, then shed into the environment via dander. This study evaluated the reduction in immunologically-active Fel d1 (aFel d1) on cat hair and dander through feeding cats a food containing egg product from chickens with anti-Fel d1 antibodies.

Method: Chickens were exposed to Fel d1 to produce eggs containing a polyclonal anti-Fel d1 IgY (IgY) which was incorporated into cat food. Hair was collected from the front, shoulders and sides of 105 cats completing a 12-week study and evaluated for aFel d1 via ELISA (Indoor Biotechnologies, Charlottesville, VA). Hair was collected during grooming, 4 times over a 2-week baseline period, then weekly during the 10-week treatment period during which cats consumed the cat food made with egg product containing IgY. Effects were analyzed using a linear, mixed effect model and ANOVA with Turkey Post-Hoc tests. (R Core Team, 2015 version 3.2.1).

Results: Baseline aFel d1 (μg/g hair) varied greatly among cats, from a mean (± s.d.) of 64 ± 21 in the lowest quartile to 533 ± 330 in the highest quartile. From week 3 onward, there was a significant reduction in mean aFel d1 with an average decrease of 47% by week 10. Cats with the highest baseline aFel d1 showed the greatest decreases.

Conclusion: Feeding cat food made with egg product containing IgY successfully reduced active Fel d1 in the hair and dander of cats, with the greatest decreases observed in cats with initially high levels. Although additional research is needed, this approach suggests a new tool for management of allergies to cats.

TP1330 | A novel patient-reported outcome (PRO) instrument assessing the side effects of peanut oral immunotherapy

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Background: Patients treated with peanut oral immunotherapy (OIT) may experience adverse reactions, particularly during updosing. We developed the Side Effects of Peanut Oral Immunotherapy Diary (SEPOD), an electronic patient-reported outcome (PRO) measure, to assess these reactions. The SEPOD is intended for daily administration in pediatric patients taking OIT for peanut allergy desensitization.

Method: The content and design of the SEPOD was informed by a review of the empirical literature, a food allergy instrument review, and meetings with three allergy and immunology specialists with experience treating pediatric patients with peanut OIT. We conducted 24 interviews with pediatric patients (6-17 years) who have peanut allergy. Patients 6-12 years of age were interviewed with their caregiver. The first 14 interviews were conducted to explore the pediatric patient experience with peanut OIT and to inform SEPOD item development; the 10 subsequent interviews were conducted to evaluate participant understanding of and ability to complete the SEPOD.

Results: Results from the literature and instrument review, allergy specialist meetings, and sponsor clinical expert advisement were used to draft questionnaire content for the SEPOD. Patient interviews confirmed SEPOD content and informed revisions. The SEPOD collects information on 23 peanut OIT side effects: gastrointestinal (GI) (4 items), dermatological (2 items), itching (5 items), nasal/respiratory (5 items), swelling (of the eye, lip, tongue, throat; 4 items), pain (of the tongue/mouth, throat; 2 items), and dizziness (1 item). The SEPOD is intended for self-report as a PRO in patients ages 12-17 years; a caregiver-administered version was developed for patients 6-11 years with an observer-report option for patients 6-8 years. The SEPOD collects the time when peanut OIT is taken and 2 hours after the reported OIT ingestion time, the diary prompts a response on the presence, severity, and duration of side effects. The following day, before peanut OIT ingestion, the diary asks about yesterday's unresolved side effects and newly occurring GI side effects.

Conclusion: The SEPOD is a new content-valid tool that could be used to assess side effects experienced by pediatric patients treated with peanut OIT.

TP1331 | Evaluation of the efficacy and safety of sublingual immunotherapy (traditional coca's extract) in the treatment of allergic rhinoconjunctivitis

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Background: Allergic rhinoconjunctivitis is a common allergic disorder that significantly affects the patient's quality of life (QoL). Sublingual immunotherapy (SLIT) is an effective and safe therapeutic approach. In countries with low socioeconomic levels, traditional coca's extracts is a cost-effective choice. This study aimed to evaluate the efficacy of homemade Coca's extracts SLIT in improving the QoL of patients with allergic rhinoconjunctivitis. Additionally, evaluate the effect of SLIT on patients' medication score and compare its efficacy and safety with the pharmacological therapy.

Method: 120 allergic rhinoconjunctivitis patients were randomly placed into two similar groups of 60 patients each. Group 1 received pharmacological therapy on regular basis, while group 2 received SLIT and as required pharmacological therapy, both groups were followed up for one year.

Results: After one year 37(61.6%) patients dropped out from group 2 while 17 (28.3%) dropped out from group 1. Initially, there were no statistically significant differences in the scores of miniRQLQ or medication scores between the two groups. Both groups showed statistically highly significant improvement in QoL ($P < 0.001$); however, improvement in group 2 was statistically significantly higher than group 1($P < 0.001$). For group 1; scores for activity, practical problem, nose symptoms, eye symptoms and others (tiredness, thirst, feeling irritable) decreased from 8.55 ± 3.643, 7.98 ± 2.600, 11.13 ± 4.394, 8.77 ± 4.795, and 10.55 ± 4.196 to 5.88 ± 3.540, 6.02 ± 3.642, 6.93 ± 4.881, 4.28 ± 4.261, 6.05 ± 4.810, respectively. For group 2, the decrease was from 7.98 ± 5.020, 8.50 ± 2.949, 11.17 ± 5.340, 8.43 ± 5.457, 9.35 ± 4.683 to 1.17 ± 1.193, 2.61 ± 2.251, 2.87 ± 2.418, 2.13 ± 2.581, 3.96 ± 2.440 respectively. Medication score of group 1 showed a mild non-significant decrease from 2.97 ± 0.18 to 2.70 ± 0.723, while, Group 2 medication score significantly decrease from 3.00 ± 0.000 to 0.38 ± 0.495. There were no severe adverse effects in any of the two groups. No statistical difference was found in the incidence of mild adverse reaction between both groups.

Conclusion: Homemade coca's extracts used in SLIT are a safe treatment that improves both qualities of life and medication sore in patients suffering from severe allergic rhinoconjunctivitis.

QoL questionnaire results			N	Mean	SD	Median	range		MW	P
At The beginning of the Study	Activity	Group 2	60	7.98	5.020	7	0	18	1.96	0.06^{NS}
		Group 1	60	8.55	3.643	8	2	15		
	Practical problems	Group 2	60	8.50	2.949	9	3	12	1.97	0.06^{NS}
		Group 1	60	7.98	2.600	8	2	12		
	Nose symptoms	Group 2	60	11.17	5.340	12.5	0	18	0.55	0.59^{NS}
		Group 1	60	11.13	4.394	12	1	18		
	Eye symptoms	Group 2	60	8.43	5.457	9	0	18	0.40	0.69^{NS}
		Group 1	60	8.77	4.795	9	2	18		
	Others	Group 2	60	9.35	4.683	9	0	18	1.38	0.17^{NS}
		Group 1	60	10.55	4.196	10	3	18		
	Total	Group 2	60	45.05	16.338	39	22	78	0.72	0.47^{NS}
		Group 1	60	45.35	11.967	40.5	19	71		
At The end of the Study	Activity Post	Group 2	23	1.17	1.193	1	0	4	5.55	<0.001**
		Group 1	43	5.88	3.540	6	1	15		
	Practical problems	Group 2	23	2.61	2.251	2	0	11	4.32	<0.001**
		Group 1	43	6.02	3.642	4	2	12		
	Nose symptoms	Group 2	23	2.87	2.418	3	0	11	3.90	<0.001**
		Group 1	43	6.93	4.881	6	1	18		
	Eye symptoms	Group 2	23	2.13	2.581	1	0	11	2.75	0.006**
		Group 1	43	4.28	4.261	3	0	18		
	Others	Group 2	23	3.96	2.440	3	2	10	1.98	0.04*
		Group 1	43	6.05	4.810	5	1	18		
	Total	Group 2	23	12.30	8.331	10	4	42	5.18	<0.001**
		Group 1	43	29.26	18.020	24	11	73		
Medication Scores	MS at the beginning of the study	Group 2	60	3.00	0.000	3	3	3	1.43	0.16^{NS}
		Group 1	60	2.97	0.18	3	2	3		
	MS at the end of the study	Group 2	24	0.38	0.495	0	0	1	8.76	<0.001**
		Group 1	40	2.70	0.723	2	1	3		

TP1332 | Development and assessment of dietitian-led counselling program for oral immunotherapy

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Background: Oral immunotherapy is a new treatment for food allergies. It consists of progressively increasing the daily consumption of allergenic proteins to induce desensitization. Allergen doses start with flour precisely weighed by the medical team. They are next increased until they reach the whole food patients need to prepare by themselves at home. Lack of palatability and/or variety in food equivalents is a frequent and non-negligible issue that can even sometime seriously threaten adherence to treatment. We created a food equivalent document and nutritional counselling program to help patients in the selection of appropriate allergens forms. We hypothesized that this nutritional intervention would facilitate the appropriate selection and dosage of food alternatives and increase parent competency and satisfaction.

Method: This was designed as an open-label randomized trial. Parents of children treated with oral immunotherapy at Sainte-Justine Hospital in Montreal, Canada were recruited and randomized to three intervention arms: A) Dietitian counselling and food equivalent documents two weeks after switching from powders to food equivalents (T1); B) Dietitian counselling at (T1) and documents received after 4 additional weeks (T2); and C) a control group with no intervention until 6 weeks (T2). Practical exam on food equivalent calculations as well as satisfaction and competency questionnaires were administered before intervention (T0), immediately after intervention at T1, at T2 and 8 weeks after T2 (T3).

Results: As of December 2018, 28 participants have been enrolled, 23 have undergone T1, 20 have undergone T2 and 13 have completed the trial. Of these, 17 (74%) parents were mothers and 16 patients were boys (70%). Their mean age was 7.1 years old (± 4.6)

and they were mostly treated for peanut (74%), milk (35%) and nuts (30%). Performance on the equivalence calculation test improved significantly after counselling and documents (+90%, $P < 0.0001$) and counselling alone (+41%, $P = 0.002$) compared to before any intervention.

Conclusion: This study clarifies the need to develop nutritional interventions to help patients manage their oral immunotherapy doses at home. Written documents are needed to achieve the full benefit of the intervention.

TP1333 | Safety of a five-step versus a six-step ultra-rush venom immunotherapy protocol

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Background: Venom immunotherapy (VIT) is the most effective treatment for hymenoptera venom allergy (HVA). There are several build-up protocols that rapidly increase the doses administered. Ultra-rush regimens are safer and more convenient for the patient, and induce protection to subsequent stings faster.

Aim: To compare the safety of a faster five-step (180 minutes) ultra-rush regimen versus the standard six-step (210 minutes) protocol.

Method: A medical records review of all the patients who underwent VIT with honey bee or wasp venom in an allergy department between January 2016 and December 2018 was performed. Data regarding demographic characteristics, HVA, sting reaction severity (according to Mueller) and adverse reactions during VIT were collected.

Results: A total of 67 patients were included; 49 (77%) male, mean age 39 (± 16) years. All completed an ultra-rush regimen: 41 (64%) with honeybee (*Apis*), 22 (34%) wasp (*Vespula*) and 1 (2%) paper wasp (*Polistes*). With respect to sting severity, 62 (92%) had grade 3 or 4 systemic reactions. Of the total, 27 (42%) underwent the five-step regimen: 6 (22%) had local reactions, 11 (41%) had systemic reactions and only 1 (9%) required adrenaline.

Systemic reactions were only observed with honeybee VIT. There were no statistically significant differences between both schedules regarding the number of patients with local reactions ($P = 0.264$) and systemic reactions ($P = 0.055$), although there was a tendency for more patients with systemic reactions during the five-step schedule. More patients required adrenaline with the six-step regimen ($P = 0.047$).

Conclusion: Different ultra-rush protocols are used for VIT. No significant differences regarding adverse effects were found between both VIT schedules, although adrenaline was used more in the patients who underwent the six-step protocol. Therefore, removal of the first step has the advantage of decreasing the time spent in the hospital, increasing patient convenience while maintaining the safety of the procedure.

TP1334 | Specific immunotherapy in adult patients sensitised to alternaria alternata

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Background: Sensitisation to *Alternaria alternata* has been widely studied in children during the last years, but not in adults to date. It is well-known that sensitisation to the aforementioned allergen is a cause of respiratory symptoms (asthma and rhinitis) as well as ocular symptoms (conjunctivitis). Subcutaneous specific immunotherapy has demonstrated its efficacy in modifying the course and evolution of allergic disease. Objective: This retrospective descriptive study was designed in order to study the clinical characterization of a group of adult patients sensitised to *Alternaria alternata*, as well as its symptomatic debut, the use of subcutaneous specific immunotherapy as an essential part of the treatment and the increasing trend of its use in recent years.

Method: A total of 228 patients were included in our study. We purposively selected only adult patients (86 patients) with respiratory allergy, who were sensitised to *Alternaria Alternata* and had been prescribed subcutaneous allergen specific immunotherapy in the last 10 years. We studied their clinical characteristics, the endurance of the treatment, and their clinical evolution.

Results: Out of the 86 total patients included in our study, 44 were women and 42 were men. 76 patients out of 86 were asthmatic, of which 41 had rhinitis and conjunctivitis associated. 8 patients out of 86 had rhinitis and conjunctivitis, and 2 patients out of 86 only had rhinitis. Persistent-mild asthma is the most frequent level compared to mild-intermittent and persistent-moderate asthma. Regarding treatment with immunotherapy, 32 patients finished the treatment, 29 are pending clinical evolution since they have not finished the treatment yet, and 25 interrupted it for different reasons. It is noteworthy that since 2015, 39 patients out of the total (86) have started treatment with immunotherapy (39/86). 59 patients out of 86 started with their symptoms when they were older than 18 years.

Conclusion: An increase in the administration of subcutaneous immunotherapy has been noticed in adult patients sensitised to *Alternaria alternata* in our work centre in the last three years. According to our results, a large proportion of patients presented their clinical debut in adulthood (patients older than 18 years). Despite the results in the present study, further studies need to be carried out in adult population.

TP1335 | Comparison of the cost of illness during symptomatic treatment and specific immunotherapy, in patients with allergic asthma to mites: The itaca study

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Background: Introduction: Most of the studies in which the cost-effectiveness of immunotherapy (IT) is analyzed, have been performed in adult patients with rhinitis, based on pharmacoeconomic models. There is a need for real world prospective pharmacoeconomic studies in asthmatic patients to compare the cost of illness before and after IT. Objectives: The comparative analyses of the cost of illness during the symptomatic treatment period (ST) and the first 6 month with IT was described.

Method: Observational study of prospective follow-up in 29 Spanish allergy departments. Patients aged 12-60 years with a confirmed diagnosis of intermittent to persistent moderate asthma due to sensitization to mites were selected. Patients followed for 6 months of symptomatic treatment (ST) and 6 months with IT, completed a diary on the consumption of healthcare and non-healthcare resources. The costs of illness during the ST versus IT period were examined. The annual costs were calculated to allow the comparison with other studies.

Results: From a total sample of 178 patients, data from the first 76 that ended the ST period were analyzed and 39 of these patients also completed 6 months of IT. The mean age was 32 years, being 19.7% of 12-18 years-old and 49.3% female. Intermittent asthma was observed in 23.7%, persistent mild in 25% and persistent moderate in 51.3%. The annual non-medical costs in the ST/IT periods were 140.6/146.2 Euros/year, the annual medical costs 1256.4/827.3 Euros/year ($P < 0.05$) and the total costs (medical and non-medical costs) of 1397/973.5 Euros/year. In the multivariate analysis of the total costs controlled by age, sex, socioeconomic level, type of asthma, presence and type of rhinitis, statistically significant differences were observed between the two periods, resulting the symptomatic period 453 Euros (95% CI 3 -903) more expensive than the period with IT ($P < 0.05$). Costs of IT were not included in the analyses as will be described by administered product.

Conclusion: These preliminary results already allow us to glimpse that IT reduces the total costs in asthma allergic to mites and, therefore, is an efficient therapeutic alternative in these asthmatic patients.

TP1336 | Mid-scale processability and characterization of the allergoidization of salsola kali allergen extracts

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Background: Saltwort (*S. kali*) is a weed with high incidence in dry regions all over the world. Its allergens have become one of the primary causes of seasonal allergy on the Mediterranean coast of Europe. The present study aims to show the feasibility of producing an allergoidized *S. kali* pollen extract adsorbed to aluminum hydroxide ($Al(OH)_3$) suited for the allergen-specific immunotherapy (AIT) of saltwort pollinosis.

Method: An unmodified allergen extract was obtained from routine production (Allergopharma). The allergoidization process comprised a treatment and subsequent two-step incubation with formaldehyde. The ensuing steps included purification via filtration and lyophilization of the drug substance. For the drug product, a co-precipitation step, including the allergoid adsorption, followed by washing and sieving of the obtained suspension, was applied. Both process parts were represented by three batches produced in a mid-scale setup. The intermediate and finished products were characterized by various physicochemical and immunological methods to assess the feasibility and reproducibility of the applied processes.

Results: The allergoidization of the native Saltwort extract resulted in a markedly increased average protein molecular weight, a shift of the isoelectric point of the proteins to more acidic values (pI < 5.1), and a strong decrease in the number of detectable intact amino groups (4.8 % compared to the unmodified extract). An approximately 10,000 times reduced IgE-reactivity of the allergoid compared to the native extract further demonstrated the success of allergen modification. Three batches of adsorbed allergoids were analytically comparable concerning the assessed parameters, including the analysis of particle size distribution and particle morphology.

Furthermore, the generated drug product batches were found to have similar physicochemical properties as routinely produced drug products derived from other plant species.

Conclusion: A reproducible mid-scale process for the manufacturing of an allergoidized saltwort pollen drug product was successfully established. The quality of the drug substance and drug product was well-comparable to routinely manufactured AIT drug products. Hence, the presented study delivers a solid basis for the next development steps of a formallergoid-based drug product for a successful and safe therapy of *S. kali* pollinosis.

TP1337 | Birch sap as a novel treatment for birch pollen allergy

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Background: Birch pollen allergy is a major health problem of growing concern, affecting the quality of life of millions of people worldwide. Current treatment approaches are often inadequate and may induce adverse side effects. Across Scandinavia, many people suffering from birch pollen allergy, report mitigation of their symptoms by consuming birch sap. However, there is no scientific evidence of whether this is a placebo or a systemic response. We *hypothesise* that birch sap contains Bet v 1 cross-reactive proteins and can be used to treat birch pollen allergy. The *purpose* of this project is to provide solid evidence for using birch sap to prevent and treat birch pollen allergy.

Method: Birch sap from Danish birch trees was collected during the tapping season and the protein content and profile analysed by proteomic analyses. Immune reactive proteins in birch sap and birch pollen cross-reactive allergens were identified by immunoblotting. The potential induction of oral tolerance to birch pollen by birch sap and consequently, the prophylactic efficacy against birch pollen allergy was determined in a Brown Norway rat model of food allergy primary prevention. Rats were given birch sap *ad libitum* for three weeks and subsequently post-immunised i.p. with birch pollen. Allergen specific IgG1 and IgE levels as well as avidity were analysed by ELISAs and the clinical reactivity assessed by an ear swelling test.

Results: Birch sap protein concentration increased over time being highest at the end of the season. No significant correlation between protein concentration and either temperature, rain, or hours of sun was observed. Birch sap contained proteins ranging from 10 to 80 kDa and Bet v 1 homologous proteins were detected by birch pollen-sensitised animals. Oral administration of birch sap resulted in decreased levels of IgG1 and IgE, as well as decreased clinical reactivity to birch pollen after i.p. post-immunisations with birch pollen.

Conclusion: These results demonstrate the presence of the birch pollen Bet v 1-homologous allergens in birch sap, thus birch sap could be the foundation for an innovative, ecological, safe and cheap method to treat millions of birch pollen allergic individuals.

TP1338 | Efficacy of specific immunotherapy in fungal allergy

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Background: Specific immunotherapy is (SIT) the treatment of choice for many allergic diseases if complete diagnostic procedures have been performed. The diagnosis of allergic disease should be undoubtedly, with complete laboratory in vitro, and allergen in vivo testing. So, it is necessary to know which allergen is accused, and the allergy should be confirmed by in vivo test. Fungal allergy if present very often, mostly in rooms with high humidity. In recent time SIT was not be recommended in common use, but today recommendation was changed. The three year experience with SLIT for fungal sensitizations was given in this paper.

Method: We followed up the patients with confirmed fungal allergy during three years of SLIT. Diagnostic procedures were performed by measurement of total IgE, PRICK skin test, microbiological analysis of skin wipe specimen, stool analysis for fungi.

Results: We followed 37 patients with confirmed fungal allergy, treated with sublingual immunotherapy (SLIT) against aspergillus (25 pts) and alternaria (12 pts). With allergic rhinitis there were 28 patients (76%), 3 patients (8%) with allergic conjunctivitis, 6 patients (16%), with skin eczema and alopecia areata. In four patient asthma was present in same time. Skin PRICK test were mandatory for all patients. The efficacy of treatment was considered according to Health- related quality of life(HRQoL). After SLIT treatment during three years we have very well answer in 28 patients (76%), well answer in 6 patents (16%), limited answer in 2 patients (5.4%), and no answer in 1 patient (0.27%). For those with limited or no answer the therapy was withdrawn.

Conclusion: Sublingual immunotherapy against fungal allergy showed well efficacy with improvement of HRQoL, if diagnostic procedures were performed correctly. It is to not hesitate to withdrawn SLIT if therapeutic answer is not satisfied.

TP1339 | Subcutaneous immunotherapy with aeroallergens - evaluation of adhesion in real life

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Background: The clinical efficacy of subcutaneous allergen immunotherapy (SCIT) requires the administration of standardized allergen extracts in adequate doses for a sufficient period of time (3-5 years). Low adherence is a critical variable, compromising the efficacy of this treatment. Objective: Assess patients (pts) adherence and identify determinant factors for the maintenance of SCIT.

Method: Retrospective analysis of medical records of pts submitted to SCIT between Jan2013-Dec2016 in our Immunoallergology Outpatient Department. Determination of the SCIT adhesion rate and characterization of the factors that motivated its suspension before the schedule time.

Results: 631 pts, 308 were excluded due to data unavailability; 323 were included (F167 (52%), mean age 30 ± 13 years (min7;max73), age group [18-30] more prevalent-45%). Average treatment time - 19 ± 13 months. 70% of the pts were in the first 2 years of SCIT;17.6% completed at least 3 years of treatment. The compliance rate for administrations/year was 93%. 45% (14%) didn't comply at least 3 administrations, with an average cumulative dose of 73.7%. 52 pts (16%) stopped SCIT before the scheduled time:F28 (54%), mean age 30 ± 9 years (min14;max48), age group [18-30] more prevalent (54%). Regarding composition, SCIT suspension for mites was predominant (73%, 17.8% of total SCIT for mites) followed by pollens (27%, 16.3% of total SCIT for pollens). No predominance of prescribing physician. Mean duration of treatment - 12 ± 6 months. 67% discontinued in the 1st year, 27.2% in the 2nd and 5.8% during the 3rd year of treatment. The most frequent reason for withdrawal was economic question (47.9%), followed by perception of no clinical improvement (23%), change to sublingual immunotherapy (11.6%), personal issues (7.7%), local reactions (3.9%), acute medical illness (3.9%) and pregnancy (2%). The most frequent cause of suspension in the 1st year was an economic question (60%), and the perception of no improvement was the most frequent reason for the next two years.

Conclusion: 16% of the pts stopped SCIT before the scheduled time, with the economic issue being the main cause in the 1st year, while the perception of non-improvement determined the adherence in subsequent years. Thus, adequate information on SCIT prescribing and rigorous monitoring of pts during the treatment can improve adherence.

TP1341 | Immunotherapy with an allergen extract of candida albicans to prevent recurrent episodes of vulvovaginal candidiasis (RVVC)

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Background: *Candida albicans* could be a commensal fungus as well as a true pathogen of areas that are highly enriched in dendritic cells (skin and mucosal surfaces). Th2-like reactivity is frequently observed in patients with *Candida*-related pathology, including symptomatic infections and allergy. Recurrent Vulvovaginal Candidiasis (RVVC) is probably the most prevalent infection caused by *Candida albicans* and, occasionally, is also produced by other *Candida* sp. or yeasts. RVVC is defined as 4 or more episodes of vulvovaginal infection in a period of 1 year. It is estimated that 75% of women will have at least one episode of VVC, 40%–45% will have two or more episodes and 5-8% of adult women will develop RVVC. No effective long-term cure has been found. Preventive strategy is necessary, but therapy is limited to the prophylactic treatment for the removal of the causative agent. There are other emerging alternatives to avoid reinfection or relapse without scientific evidence of its efficacy. Because the Th2-like reactivity found in *Candida*-related pathology, the use of *Candida*-specific allergen immunotherapy could be an approach to treat RVVC.

Method: Patients: 6 women (median age 39 years, range 25-51) were treated. Median of RVVC episodes in the 12 months prior to treatment was 6 (range 4-8). RVVC was diagnosed by evaluation of clinical symptomatology, recurrent vaginal fluid culture and *C. albicans* identification. All had been previously treated with topical and systemic antifungal preparations by the GP and/or the gynecologist. Only one patient had positive skin prick test with an extract of *C. albicans* and measurable specific IgE (CAP 3.49 KU/L). All had positive delayed reaction to the intradermal test.

Treatment: All received individualized subcutaneous immunotherapy (Alutek®, Inmunotek, SL, Spain) with aluminum hydroxide-adsorbed allergen extract of *Candida albicans*. The concentration was 10,000 TU/mL. The schedule of administration was 0.2 mL in one arm followed by 0.3 mL after 30 minutes in the other arm the first day. Maintenance was 0.5 mL monthly.

Results: After 3 months of treatment, patients are free of symptoms. No systemic adverse events with this immunotherapy have been experienced.

Conclusion: Immunotherapy with individualized *Candida albicans* allergen extract (Alutek®) is safe and effective. This treatment could be an effective strategy to reduce the frequency and duration of these recurrent vulvovaginal infections.

TP1342 | A rare complication of allergen-specific immunotherapy: Eczema herpeticum

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Case report:

Introduction: Allergen specific immunotherapy(AIT) using house dust mite extracts has been performed mainly with patients of asthma and allergic rhinitis. The only treatment that can be good on the causes of allergy. Atopic dermatitis is a chronic, inflammatory skin disease with intractable pruritus. unfortunately, the exposure to aeroallergens, like house dust mites and pollens, can cause increase of AD, in children and adults and also AIT can be used for AD.

Case: An 18-year-old woman was diagnosed with asthma, allergic rhinitis and atopic dermatitis for the past 10 years. Her asthma was under control with the use of salbutamol inhalation in the spring as needed. She was using nasal antihistamines and nasal steroids for allergic rhinitis. In the skin prick test, house dust mite, grass pollen, dog and rye sensitization were present. It was decided to initiate subcutaneous allergen-specific immunotherapy for pre-season grass pollen and house dust mite for the patient who did not want to use drugs for a long time. Routine tests were sent before treatment, kidney function tests, liver function tests were normal. In other tests; Total IgE:1078 IU/ml, specific IgE (D1 ptero):42.7 KU/L and specific IgE (D2 farin): 77.1 KU/L. Allergen-specific immunotherapy was initiated for pre-season grass pollen and house dust mite simultaneously according to the cluster dosing schedule. After one week, the patient was admitted with the complaint of increased skin lesions after the first dose of treatment. The patient was also found to have increased atopic dermatitis and lesions were infected. Allergen-specific immunotherapy was stopped.

She was consulted with dermatology, in the examinations; herpes simplex type 1 IgM: negative, herpes simplex type 1 IgG: 16.43 positive (, anti HCV: negative, HBSAG: negative, Anti-HBS: negative, HIV Ag/Ab: negative, VDRL-RPR (negative), crp: negative. There was no reproduction in wound culture. Considering eczema herpeticum, amoxicillin + clavulanic acid 1000 mg 2 * 1 oral, acyclovir 250 mg 3 * 1 iv, topical treatment was started. Skin lesions regressed in the follow-up of the patient.

Outcome: Subcutaneous allergen-specific immunotherapy may be used in the treatment of atopic dermatitis, but we would like to present on this case that severe skin lesions may develop due to treatment.

TP1343 | Anti-allergic and anti-inflammatory effect of Hizikia fusiformis

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Background: The extract of Hizikia fusiformis (H. fusiformis) is known to exhibit anticancer, anti-atopic and antioxidant activities. We aimed to investigate the extract of H. fusiformis on allergic rhinitis inflammation in vitro and in a mouse model.

Method: RAW 264.7 macrophage cells were incubated in the presence of different concentrations of viscozyme component of H. Fusiformis (1, 2, 5, and 10 μg/mL) and changes in expression of pro-inflammatory cytokines were evaluated. In vivo experiment, the 4-week-old BALB/c mice were randomly assigned into 4 groups: group A, control group (n = 9); group B, allergic rhinitis group (n = 10); group C (n = 10) received 300 mg/kg H. Fusiformis during nasal challenging period; group D (n = 10) received 600 mg/kg H. Fusiformis during general sensitization period and 300 mg/kg H. Fusiformis during nasal challenging period. Allergic inflammation was made with ovalbumin (OVA) and alum then challenged intranasally with OVA. H. fusiformis was intraperitoneally administered 3 hr before the OVA administration. Multiple parameters of allergic inflammation were evaluated.

Results: The viscozyme component of H. Fusiformis downregulated the GM-CSF, iNOS, VEGF, COX-2 mRNA expression in a lipopolysaccharide (LPS)-induced RAW 264.7 cells. The signal intensity of p-pNF-κB 65, p-pIkBa, p-p38, and p-p44/42 protein activated by LPS was ameliorated by H. Fusiformis. Moreover in animal study, H. fusiformis administrated groups C and D showed significant inhibitory effects on nasal symptoms, IL-13 mRNA expression and eosinophil infiltration/goblet cell hyperplasia in the nasal tissue; OVA specific IgE production in serum. In group D, H. fusiformis treatment downregulated IL-4, IL-5, IL-13, TNF-α and IL-10 cytokine expression in splenocyte culture as well as significantly decreased IgG_{2a}, IgG_1 levels in serum compared with group B. However, the expressions of IL-5, IFN-γ and FOXP3 mRNA did not change in groups C and D.

Conclusion: *H. fusiformis* could induce anti-allergic inflammation by suppressing the Th 2 cytokine production (IL-13) locally and systemically, OVA-specific IgE formation, and goblet cell hyperplasia/eosinophilic infiltration in a mouse model of allergic rhinitis. Thus, *H. fusiformis could be considered as a potential therapeutic agent in treating allergic rhinitis.*

TP1344 | RNA and DNA drugs based on prolonged acting liposomes

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Background: One of the key problems of modern biomedicine is the prolongation of the biological effects of drugs. This problem is particularly prevalent among the new generation of products, which include DNA and RNA molecules. Nucleic acids cannot independently penetrate into the cells to render their biological effect, so it is necessary to include special carriers such as liposomes. Surface modification of liposomes with PEG molecules is currently the main approach to creating a hydrophilic barrier around a transport particle that prevents interaction with blood components and macrophage capture, prolonging the circulation time of drugs in the blood. The aim of this work was analyzing how PEG can influence the effectiveness liposome/gene complexes in vitro and in vivo.

Method: Liposomes preparation (including PEG-modified liposomes); examination of transfection efficacy by luciferase assay and cotransfection experiments, followed by PCR; study of liposomes cytotoxicity by MTT-test; pharmacokinetic studies.

Results: The modified liposomes were produced by addition of 2, 4, 5, 6, 8, 10 and 15 mol. % of PEG during thin lipid layer preparation step. Influence of PEG on the liposome's ability to carry and release genetic material in cells was evaluated by the luciferase test (to study transfection efficiency of plasmid DNA) and cotransfection, followed by PCR (to evaluate siRNA transfection efficiency) for two cell lines HEK293 and HepG2. Both cell lines revealed that the best results are achieved at 2 and 6 mol. % PEG liposomes after 24 hours of incubation. It was found that after an extra day of incubation, the transfection efficiency increases almost twofold. The pegylated liposome transfection efficiency begins to exceed the efficiency of non-modified liposomes on both cell lines. After 48 hours, the best results are obtained not only for 6 mol. % PEG liposomes, but also for the 4 and 5 mol. %. Studies of liposomal dispersions cytotoxicity showed a reduction of toxicity in liposomes with an increase of PEG ratio derivative to general liposome composition. During the pharmacokinetic studies the prolongation effect of modified liposome was also proved.

Conclusion: It was shown that the insertion of hydrophobic PEG derivatives in liposome composition reduces the cytotoxicity of modified cationic liposomes and prolongs their action.

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TP1345 | Feasibility of studying the changes in relative distribution of allergen specific antibody isotypes overtime

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Background: Allergen specific immunotherapy is the only available disease-modifying treatment for allergic patients. Proteomics offers a novel approach to study potentially hundreds of proteins and peptides using little amounts of a single biological sample, which can provide an informative measure of multifactorial diseases. Recently, several strategies using mass spectrometry (MS) have been developed, especially for the relative and absolute quantification of proteins such as the novel tandem mass tag (TMT). This technique allows distinct labelling of multiple peptide samples with isobaric chemical tags with same molecular structure and mass. Nevertheless, each tag releases a unique signal ion when fragmented in a mass spectrometer. MS^2 intensities from each tag represent the relative abundances of the peptide in each sample.

Method: The objective is to study the feasibility and optimize the protocol to measure the changes in relative distribution of allergen specific antibody isotypes overtime by quantitative mass spectrometry. All allergen specific antibodies from patient serum were enriched through the binding to biotin-conjugated allergens captured by magnetic beads. The protein eluates was digested to peptides and labelled with Tandem Mass Tags (TMT). Labelled peptides from several time points and conditions were mixed and subjected to LC-MS/MS for the identification and quantification of antibody isotype distribution overtime.

Results: We successfully developed the protocol (with low serum amounts, 100-200 μL), repeatedly identified and quantified of broad range of allergen specific immunoglobulins IgG1, IgG2, IgG3, IgG4, IgE, IgA1 and IgM. Finally, with success, applied the TMT method, obtaining the proper peptide ratios according to the samples used.

Conclusion: This methodology optimization can be an important improvement in the study of the changes in distribution of several allergen specific antibody isotypes simultaneously during different pathological or treatment situations and studies overtime. The strongholds are that small amounts of plasma or serum are used to obtain measurements of several allergen specific antibody isotypes simultaneously indicating the antibody response changes during immunotherapy.

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TP1346 | The role of health visitor in a demanding clinical protocol

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Background: Health Visitor (HV) as a research team member has an active role in designing and successful completion of a clinical protocol. This report is a detailed description of HV's responsibilities and actions during the research study CURE, a-European Horizon 2020 project, aiming to characterize and investigate the role of the microbiome in patients with obstructive respiratory diseases.

Method: Pediatric and adult patients with a medically confirmed diagnosis of obstructive respiratory disease, and matched healthy controls were recruited, following signed informed consent. The HV has informed participants in detail via telephone about the study timeplan, including all visits and procedures in predefined time points. HV has contributed in obtaining biological samples at the following time points: 1st day (0, 5, 8 hours), 2nd, 4th, 7th and 15th and 27th-31st days after inclusion. HV trained children and adults in recording daily symptoms by hard copies and e-diaries and lung function with spirometers. The study continues with the prospective follow-up of participants for one year with regular sampling and monitoring symptoms.

Results: The participants were 22 asthmatics and 11 healthy (children: 12 ± years and adults: 35 ± years). The HV emphasized the importance of participating in the study and the necessity to fully comply with the sample timetable. The HV acted as an interface between the medical research team and the participants, supporting and empowering the latter to commit to the study. HV was responsible of keeping the records and ensuring the compliance with the new General Data Protection Regulation. Follow-up sampling was mainly processed with home visits by the HV while overall communication was systematically recorded.

Conclusion: Achieving adherence to demanding protocols is essential towards ensuring the overall success and scientific value of clinical studies. HV's coordination between participants and the medical research team is essential in effectively completing the protocol.

TP1347 | Care continuity for children with asthma- the willingness of primary caregivers

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Background: Continuity of Care (COC) is one of the essential components of the asthma management. We investigated explicitly a main caregiver/ parent's attitude toward COC and their willingness to pay. We also analyzed the COC differently affect health outcome between children with/ without asthma, and compare whether asthmatic children's caregivers/ parents are more willing to spend time or pay money to maintain continuity.

Method: A cross-sectional survey was conducted during Aug.2017 to Feb.2018. Study subjects were collected from pediatric outpatient clinics in 6 different hospitals and local clinics in Taiwan. There were 825 people included, of which 149 were parents of asthmatic children. The post-stratification weighting adjustment was utilized to calculate population estimates representative of pediatric patients. The coarsened exact matching was performed to match the basic demographic characteristics of parents and children. The relationship was examined between a parent's concept of COC and their willingness to pay. Negative binomial regression was used to estimate the effect of provider continuity level on children's emergency department visits and hospitalization. The multivariate logistic regression was used to compare the willingness to pay for parents with asthma and non-asthma children.

Results: More than 80% of parents believed that COC was important to their children. 47% of parents were willing to spend 30 minutes to maintain provider continuity and only 38% of parents willing to pay more than 300NT dollars per month for COC. A higher provider continuity level, paying attention to continuity and trusting the pediatricians were associated with higher willingness to pay for COC. Asthmatic children who changed physicians had higher risk of hospitalization than non-asthmatic children (IRR = 2.00 vs IRR = 0.53). Parents of asthmatic children were not significantly more willing to pay for the COC than parents of general children, unity level on children's emergency department visits and hospitalization. The multivariate logistic regression was used to compare the willingness to pay for parents with asthma and non-asthma children.

Conclusion: Even though regular physician visits could reduce the risk of hospitalization for asthmatic children, the willingness to pay for asthmatic children's parents did not significantly higher than the parents of non-asthmatic children. The parents should be educated for the importance of provider care continuity.

TP1349 | History of asthma and lung cancer risk: A population based cohort study

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Background: We examined the association between doctor-diagnosed asthma and lung cancer from a population-based cohort. We also investigated if allergic and non-allergic asthma played a different role in lung cancer development.

Method: From Taiwan National Health Insurance Research Database, we included patients who were initially diagnosed with asthma (ICD-9-CM 493.X) between January 1, 2000 and December 31, 2005. These subjects were defined as the "asthma cohort". Controls were matched by age, gender and index day at a ratio of 1:4 (case: controls) over the same time period selected from the NHIRD. Further, we categorized asthma cohort patients into two groups according to the immunoglobulin E test, namely allergic and non-allergic groups. All subjects with a history of lung cancer prior to or within the first 2 year of the index day were excluded. The 2 cohorts were followed at least 5 years until either the development of lung cancer. The stratified cox proportional hazards model was used to determine the hazard ratios(HRs) of subsequent lung cancer among asthma and control cohorts. Covariates used in the models included age, gender and comorbidities. The Kaplan-Meier method was used to determine the cumulative incidence of lung cancer.

Results: Asthma was significantly associated with lung cancer development (aHR = 2.45, 95% CI = 2.25-2.67, P < 0.0001).After stratification by allergic and non-allergic asthma, there was no different in lung cancer development (aHR = 2.39, 95% CI = 1.87-3.04, P < 0.0001 and aHR = 2.45, 95% CI = 2.24-2.69, P < 0.0001).

Conclusion: History of asthma may increase the risk of lung cancer, after consideration of potential confounders. There was no different between allergic and non-allergic asthma.

	Non-Allergic asthma		Allergic asthma	
	Adjust HR (95% CI)	P value	Adjust HR (95% CI)	P value
CASE vs CONTROL	2.45 (2.24-2.69)	<0.0001	2.39 (1.87-3.04)	<0.0001
Age	1.03 (0.92-1.15)	0.5747	1.11 (0.79-1.55)	0.5418
Emergency	1.00 (0.96-1.05)	0.8469	0.99 (0.95-1.04)	0.7997
Inpatient	1.03 (0.97-1.09)	0.3800	0.98 (0.88-1.09)	0.7330
Comorbidities				
Congestive heart failure	1.12 (0.94-1.33)	0.2248	0.83 (0.48-1.45)	0.5099
Hypertension	1.07 (0.95-1.21)	0.2930	1.17 (0.82-1.68)	0.3774
Atrial fibrillation	0.77 (0.57-1.03)	0.0805	1.17 (0.49-2.78)	0.7278
Diabetes	1.01 (0.91-1.12)	0.8246	0.77 (0.56-1.07)	0.1172
Hyperlipidemia	1.16 (1.02-1.30)	0.0199	1.37 (0.98-1.92)	0.0621

TP1350 | Occupational asthma in a floriculturist patient

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Case Report

Introduction and Objective: Employees whose work involves contact with flowers are exposed to different occupational risks, which can trigger sensitization or exacerbation of preexisting allergic diseases. Here we present the case of a floriculturist patient with occupational asthma, getting an adequate response after suspending occupational exposure.

Clinical Case: Patient referred by Pulmonology with late-onset asthma. Due to the exacerbation of symptoms and episodes of crisis that the patient report to with some flowers, an aeroallergen prick test was performed with a negative result. A prick test was carried out, with the plants involved.

Results: The positive prick by prick results were: 3 mm for yellow chrysanthemum petal; 4 mm for petal and 3 mm for the stem of Hanson (or violet pompom). A marked improvement of the bronchial symptoms and spirometry was acquired after retiring from the work area, without reversibility to B2, even with steroid and long action B2 dismantling

Conclusions: The timely intervention and specific triggers identification in the occupational allergic disease can generate successful results in different aspects such as the life quality of the patients, their labor reintegration, and the economic burden reduction on the health system.

Spirometry

28/08/2017		TEOR	PRE#1	%Teor	PRE#2	PRE#3	POST#1	% Teor	% Cam
FVC	L	2.94	3.22	109	3.21	3.18	3.39	115	5
FEV1	L	2.49	2.04	82	2.05	2.02	2.29	92	12

02/10/2018		TEOR	PRE#1	%Teor	PRE#2	PRE#3	POST#1	% Teor	% Cam
FVC	L	3.20	3.29	103	3.20	3.17	3.28	102	0
FEV1	L	2.61	2.28	87	2.25	2.23	2.39	91	5

TP1351 | From asthma to hypereosinophilic syndrome with cardiac involvement - a case report

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Case report: Hypereosinophilic syndrome (HES) consists in persistent peripheral eosinophilia associated with tissue damage. Numerous systems may be affected and therefore clinical presentation is unspecific. Idiopathic HES is a diagnosis of exclusion.

A 25-year-old man with history of asthma and isolated bronchospasm following ibuprofen administration in early childhood presented with complaints of fatigue, dyspnea at rest and nonproductive cough. He had high respiratory rate and room air spO2 was 91%. Blood gas analysis revealed hypoxemia and hypocapnia. Laboratory testing revealed elevated eosinophil count (15 300/μL), troponins, NT-proBNP as well as IgE (>3000 UI/mL). Electrocardiogram (ECG) revealed ST segment depression and T wave inversion in V4 to V6, II, III and aVF, and echocardiogram demonstrated left and right ventricular hypertrophy with normal ejection fraction. Ground glass opacities in both lower lobes were present on Chest CT scan.

Eosinophilic myocarditis (EM) was assumed as part of HES and the patient was started on high dose corticosteroid therapy. Within 2 days his symptoms started to improve and at three-weeks follow-up the eosinophil count was normal (4000/μL). Cardiac magnetic resonance showed an area of subendocardial delayed enhancement in the apical segments, compatible with tissue fibrosis. Steroids were continued with tapering regimen.

Cardiac involvement develops in approximately 20% of patients with HES and EM may occur, representing the major source of morbidity and mortality. Clinical presentation has a wide spectrum, ranging from asymptomatic to cardiogenic shock, and laboratory/ECG findings may mimic acute coronary syndrome, as in the present case. Cardiac magnetic resonance is currently the gold standard in non-invasive diagnosis of myocarditis. High index of suspicion and early detection including exclusion of secondary causes of eosinophilia are vital, since prompt institution of steroid therapy has a dramatic improvement in the patient's prognosis.

TP1352 | The relationship between viral infections and clinic in children hospitalized with the diagnosis of lower respiratory tract infection

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Background: Acute Lower Respiratory Tract Infection (ALRTI) is one of the leading cause of hospitalization in children. Viruses are the most frequent pathogens. The aim of this retrospective study was determine the viral etiology of ALRTIs and clinical characteristics of hospitalized children.

Method: This study population comprised patients who were diagnosed and hospitalized with ALRTIs between March 2016 and February 2017. Clinical characteristics of the patients were evaluated with their medical records. Specimens from patients consisted of nasopharyngeal aspirates (NPA) taken from each patient and respiratory viruses were detected by reverse transcription polymerase chain reaction (RT-PCR) in microbiology reference laboratory of Republic of Turkey Ministry of Health General Directorate of Public Health.

Results: A total of 450 hospitalized children diagnosed with ALRTIs. One hundred and forty nine children were excluded who had no NPA samples due to technical reasons and thirty seven children were excluded who had incomplete medical records. Two hundred and sixty four (56.1% male) children were included in this study. Mean age was 19.75 ± 32.02 (minimum 0.39, maximum 213) months. Two hundred and five patients (77.7%) were under 2 years old. Forty two patients (15.9%) were aged 2-6 years and 17 patients (6.4%) were aged 6-18 years. Among the age groups, male gender was significantly higher in the patients who were under 2 years old ($P = 0.033$). There was no significant difference hospitalization between the age groups in clinic of pediatrics and intensive care unit ($P = 0.3$). A single virus was detected in 161 patients (74.2%) and 35 (13.3%) were multiple viral infections. When compared with age groups, the viral agent was detected in 79.5% of patients under 2 years of age, 69% of patients aged 2-6 years and 23.5% of patients aged 6-18 years and the difference was

statistically significant ($P < 0.001$). Respiratory syncytial virus (RSV) was most frequently detected in under 2 years of age but it wasn't detected in patients aged 6-18 years.

Conclusion: In hospitalized patients, RSV was the most frequent agent in ALRTIs but RSV wasn't detected in patients aged 6-18 years. Male gender was significantly higher in the patients who were under 2 years old.

TP1353 | Mepolizumab for chronic eosinophilic pneumonia – maximizing its benefits

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Case Report:

Background: Mepolizumab, a monoclonal anti-IL5 antibody, reduces the production and survival of eosinophils. In Europe, its licensed indication is severe eosinophilic asthma. Evidence-based knowledge on chronic eosinophilic pneumonia (CEP) is still limited. We present 2 cases of asthma and concomitant CEP successfully treated with mepolizumab.

Case 1: 54-year-old woman, non-smoker, with history of allergic asthma, rhinitis, pansinusitis and nasal polyposis diagnosed with CEP in 08/2012. Systemic steroid (prednisolone 1 mg/Kg/d) was started with rapid clinico-radiological improvement. Two relapses (11/2012, 02/2017) requiring hospital admission were identified upon steroid tapering. Long-term maintenance dose of 10 mg/d was needed. In 12/2017, the patient was referred to our hospital. She had severe uncontrolled asthma despite GINA step 5 therapy. Blood eosinophil count was 2530/uL. FeNO was > 300 ppb. Serum ANCA were negative. Spirometry revealed a mild obstructive disorder and DLCO was 75%. Chest HRCT showed airway centered, upper lobe predominant nodular opacities and bronchiectasis. Mepolizumab 100 mg every 4 weeks was started in 07/2018. Eight weeks later, respiratory symptoms markedly improved, blood eosinophil and FeNO levels decreased to 230/uL and 157 ppb, respectively and pulmonary function remained stable. Steroid dose was maintained due to *de novo* idiopathic thrombocytopenic purpura not attributed to mepolizumab.

Case 2: 21-year-old woman, non-smoker, with history of non-allergic asthma, rhinitis, pansinusitis and sensorineural hearing loss diagnosed with CEP in 08/2015. Systemic steroid (prednisolone 0.6 mg/Kg/d) was initiated with disease remission. Three relapses (10/2016, 08/2017, 04/2018) occurred upon steroid discontinuation. After last relapse, she kept productive cough, dyspnea on exertion and fatigue despite GINA step 5 therapy with a steroid maintenance dose of 10 mg/d. Blood eosinophil count was 160/uL. FeNO was 14 ppb. Serum ANCA were negative. Spirometry was normal and DLCO was 68%. Chest radiography was unremarkable. Mepolizumab 300 mg every 4 weeks was started in 07/2018. Eight weeks later, respiratory symptoms were controlled and steroid dose was gradually reduced to 5 mg on alternate days.

Discussion: Mepolizumab might be considered an effective steroid-sparing agent in CEP improving respiratory symptoms and markers of eosinophilic inflammation. Further studies are needed to clarify its potential value in preventing CEP relapse.

TP1354 | Perception of allergic rhinitis: Use of the brief illness perception questionnaire

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Background: Individual perception of a chronic illness is a driver of patient's behaviour that may impact the treatment outcomes. This important factor in allergic rhinitis (AR) has been addressed in the PETRA study, designed to assess the management of patients and their knowledge about RA.

Method: PETRA was an observational, cross-sectional, multicentre study conducted in France by general practitioners (GPs), which included adult patients with AR. The perception of AR was assessed using the Brief Illness Perception Questionnaire (BIPQ). BIPQ was validated in several chronic diseases, including asthma. The overall score is summed from the 8 items on a 0-to-10 scale so that the highest score, the worst illness perception. Factors associated with AR perception were analysed in univariate analyses, then tested in a step-by-step logistic regression model.

Results: A total of 687 GPs participated in PETRA and included 1929 patients with analysable data between May and October 2017 (women: 50.2%, mean age: 39 ± 14 years). They had intermittent (46.2%) or persistent (52.3%) AR; 14.1% also had a diagnosis of asthma; 71.7% had a non-controlled AR (ARCT score < 20). The mean BIPQ score was 4.8 ± 1.0; 53.6% of patients had a good perception (BIPQ < 5), 44.6% had a poor perception (5 ≤ B-IPQ < 7) and 1.8% had a very poor perception (BIPQ ≥ 7) of their illness. In the multivariate analysis, the factors significantly associated with a poor perception of AR were the presence of ENT complications (OR: 1.504), important or moderate nasal pruritus (OR: 2.609 and 1.792 respectively), uncontrolled AR (low ARCT score, OR: 1.357) and asthma (OR: 1.518). Factors significantly associated with a very poor perception of AR (BIPQ > 7) were asthma (OR: 5.065), allergic keratitis (OR: 9.6) and uncontrolled AR (OR: 1.890). Patients with mild AR symptoms had a better perception of their illness than those with moderate to severe symptoms. A strong negative correlation was observed between the BIPQ and ARCT scores: the poorer the perception, the less the AR control. Moreover, 84.9% of well-controlled patients had a good illness perception, *versus* 41.1% of the non-controlled patients.

Conclusion: Although no causal relationship can be drawn of this cross-sectional study, enhancing perception of AR could perhaps benefit to patients and lead to a better control of symptoms. GPs, as front-line health professionals to patients, are key players in improving the cognitive representation of AR.

TP1355 | Chronic cough with skin rash as presenting symptoms of eosinophilic inflammation related with follicular variant peripheral T cell lymphoma

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Case report: Lymphoma has been known as a rare cause of incidentally detected peripheral blood eosinophilia. Sometimes, T-cell lymphoma can present as hypereosinophilic syndrome (HES) characterized by persistent eosinophilia, and multiple organ involvements. While most cases of pulmonary involvement of T-cell lymphoma related HES were eosinophilic infiltration of lung parenchyma, bronchial infiltration of eosinophils without parenchymal infiltrations has not been reported. Here we report a case of follicular variant peripheral T-cell lymphoma which presented as a chronic cough in the form of chronic eosinophilic bronchitis, skin rash and peripheral blood hypereosinophilia.

A 62-year-old female visited allergy clinic for the evaluation of a chronic cough and generalized skin erythematous papules which lasted for 18 months. Persistent peripheral blood eosinophilia, more than 3000 cells/microliter, was noted from the initial lab tests at the primary clinic. Cervical and inguinal lymphadenopathies aggravated along with dermatologic symptom. Oral corticosteroid therapy temporarily relieved symptoms, but they recurred during the tapering period. While simple radiography of the chest was normal, chest CT revealed bronchiolitis in both lungs and mid esophageal thickening. Although spirometry, methacholine bronchial provocation test and exhaled nitrate oxide level were normal, induced sputum analysis showed an elevated fraction of eosinophils of 26%. Bone marrow aspiration demonstrated normal cellularity with normal myeloid series. Genetic tests like JAK2, CML Major/Minor, BCR/ABL, PDGFRA mutation were all negative. Pathologic evaluation of inguinal lymph node biopsy showed findings compatible with follicular variant peripheral T-cell lymphoma. After 6 cycles of CHOP chemotherapy, there was a resolution of cough, skin lesions, peripheral blood eosinophilia and the thickening of the bronchial tree, esophagus and lymph nodes.

TP1356 | The beliefs about allergic rhinitis and its treatment options from people with and without allergic rhinitis in the central region of Thailand

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Background: Allergic rhinitis (AR) patients have been suffering from the symptoms which have substantially negative impacts on their quality of life. Besides modern medicines, many patients use alternative approaches, which sometimes were misconception. This study aims to explore and compare the beliefs about AR and its treatment options between two different groups; control and AR patients group. So the result could guide us towards patient care improvements.

Method: This cross-sectional study investigates the beliefs from people residing in the central region of Thailand. Most respondents are from 3 provinces namely Pathum Thani, Bangkok and Ayutthaya. Using a self-reported questionnaire which consists of 3 parts; respondents' personal profile, the International Study of Asthma and Allergies in Childhood (ISAAC) questions and the beliefs about AR and its treatment options. ISAAC is a standardized methodology which this study applies for identifying respondents into either control or AR group. Data from 518 respondents aged between 18-80 years old were collected.

Results: From a total of 518 respondents, 311(60.0%) respondents were identified as AR group. Among AR group, only 51.4% were aware of AR and only 40.2% were treated. Many respondents from both groups share the same false beliefs (P-value > 0.05). More than 50% of both groups believe that having parents with AR increase risk of AR in their children and AR is caused by low immunity. More than 35% of both groups believe that AR is constant over a lifetime and can be fatal. More than 25% of both groups believe that prolonged use of Anti-histamine drugs can cause drug resistance and using intranasal steroid makes nasal mucosa thinner. AR group shows significantly higher percentage of beliefs than the control group (P-value < 0.05) that eating Kariyat (Andrographis paniculata), vitamin C and using herbal inhaler can relieve AR symptoms.

Conclusion: Almost half of AR patients lack of awareness of their AR symptoms. Both control and AR groups have false beliefs about AR and its treatment options; which AR group has significantly higher percentage of false beliefs in some issues. Therefore, health literacy about AR and its treatment options should be promoted in order to improve patient's care.

TP1357 | A retrospective cohort analysis of the effectiveness and safety of SCIT and SLIT. Clinical presentations

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Case report: The analysis of 350 patients on ASIT (pollen allergy), including 58 patients on SLIT- data from one reference center experience. The effectiveness of treatment was monitored by RTSS, RMS questionnaires, AST test results: more than 95% of patients noted a positive trend in a reduction or absence of symptoms of bronchial asthma, allergic rhinitis and/or conjunctivitis during the pollen season of the causal allergen, reducing the anti-inflammatory therapy need. The vast majority of side effects were local reactions: itching at the injection site, local hyperemia, local edema.

We present 2 cases of systemic reactions during ASIT and SLIT:

Patient A, 45 y/old. Allergic rhinitis and conjunctivitis. Sensitization to birch pollen, component molecular diagnostics: BetV1(100 U/mL (N 00-0.34), the patient was administered ASIT sublingually (steel birch pollen), when the dose was set at step 300IR, 30 minutes after the administration, the blood pressure 80/40, pain in the abdomen, vomiting - introduction of adrenaline, glucocorticoids, antihistamines. A retrospective analysis the examination data revealed an erosive lesion of the distal third of the esophagus, gastroesophageal reflux.

Patient,F., 39 y/old Bronchial asthma. Allergic rhinitis and conjunctivitis with seasonal exacerbations. Sensitization to wormwood. During ASIT (allergoid wormwood, sc) there were no local and general reactions to the administration of the medication.

At 40 min after the allergoid administration at a dilution of 10^{-1} 0.3 mL, the patient complained of dizziness, redness of the face, with hemodynamics preserved, blood pressure to 60/40.

In the frame of the systemic(anaphylaxis) therapy, the introduction of adrenaline, glucocorticoids.

The additional retrospective anamnesis showed the disruption of the elimination compliance the day before the next injection(herbal sauna, minimum alcohol intake). As part of anaphylaxis (within 2 hours after the developed reaction), the increase of the total tryptase level was registered x 2N.

Results of component diagnostics: W231 17.4 U/mL, W233 54.3 U/mL

The safety of ASIT therapy, regardless of the method, depends on the individually correct selection of the patient. Component allergy diagnosis may be helpful in identifying patients at high risk of severe allergic reactions (class of cross-protein LTP). Serum total tryptase level could serve as an additional marker in the differential diagnostic algorithm.

TP1359 | A two-site immunoassay for the quantification of lolium perenne grass pollen allergen, Lol P 1

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Background: Grass pollen is a significant cause of allergy and there are numerous commercial extracts for the diagnosis and treatment of grass pollen allergy. Group 1 grass allergens are considered major allergens as many people are sensitised to these proteins. As such, the detection and measurement of group 1 grass pollen allergens may be important for standardising allergen products and monitoring environmental exposure. Our aim was to develop a two-site immunoassay for the quantification of *Lolium perenne (Ryegrass)* grass pollen allergen, Lol p 1.

Method: Natural Lol p 1 was purified from Ryegrass pollen extract and used to immunise mice for monoclonal antibody development. Antibodies were screened and suitable pairs identified to develop a two-site ELISA against Lol p 1. Samples including diagnostic and therapeutic products were analysed using the assay to assess specificity.

Results: The assay LOD was determined to be 7.81 ng/mL. Assay accuracy and reliability was strong, with recovery being ± 30% as well as intra and inter-assay variability < 15%. Specificity testing with a number of grass pollen extracts revealed cross-reactivity with grass pollen extracts from closely related species, including Phleum pratense. Purified allergens were also tested which revealed cross-reactivity with homologous group 1 grass pollen allergens.

Conclusion: We generated a sensitive two-site at ELISA for the quantification and detection of group 1 grass pollen allergen, Lol p 1. The assay was demonstrated to have cross-reactivity to other group 1 grass pollen allergen and extracts from related species, including Phleum pratense / Phl p 1. The assay has applications in standardisation of therapeutic and diagnostic preparations as well as monitoring environmental exposure.

TP1360 | The lived experience of nasal polyps – the current understanding of the patients' perspective

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Background: In patient-centered drug development the patient experience of a disease needs to be fully understood so that meaningful treatments, from the patient perspective, can be developed. In addition to clinical input, the patient perspective also serves to inform which endpoints should be assessed in clinical studies. The aim of this study was to conduct a review of published qualitative research and supplementary internet sources (e.g., online patient blogs/forums) to explore the documented patient experience of nasal polyps (NP).

Method: A targeted search of MEDLINE, Embase and PsycINFO databases was conducted to identify publications relating to the symptoms and health-related quality of life (HRQoL) impacts of NP. A supplementary review of online patient blogs/forums was also conducted to identify any additional qualitative information.

Results: The database search generated 319 abstracts from which three articles met the inclusion criteria and were retained for full-text review. The articles reported on studies conducted between 2015 and 2016 in the UK and Canada and included male and female, adult patients. Nine NP symptoms (nasal congestion, swelling, tightness and pain, runny nose, loss of smell, mucus, dry throat/mouth and headaches), five triggers of NP symptoms and 23 HRQoL impacts were reported across the publications.

A total of four patient blogs/forums were identified for review. These provided confirmation of the majority of symptoms identified within the published literature; however, additional symptoms (e.g. nose bleeds, sneezing, visible polyps) and impact concepts (e.g. gagging, sleep apnoea, frustration) were also identified.

Conclusion: Traditional literature searches yielded very few articles informing on patient-centered qualitative research in NP. Findings were supplemented with patient blogs/forums as a novel and alternative source of information which generated additional insights. Findings indicated that most symptoms of NP were nasal symptoms however some non-nasal symptoms were also reported. Collectively, these symptoms had a significant impact on the lives of patients with NP. Given the paucity of qualitative information about the lived experience of NP there remains considerable scope for further qualitative research in this field.

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TP1361 | Novel patient centric approach to understand the patient experience of nasal polyps

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Background: Currently, there are limited qualitative data regarding the experience of patients with nasal polyps (NP).

Method: Qualitative interviews were conducted with patients with severe, recurrent bilateral NP, and history of at least one surgery for NP. The aim of the interviews was to identify NP experiences that are important to the patient as well as the language used to describe the disease experience. A smartphone/tablet app-based task was used over a 10-day period to explore the patient experience of NP in 'real time' and capture any variability that exists in these experiences in a subset of the interview patients. Responses to the app task were collected using a variety of mediums (i.e., video, audio, text and photographic responses with captions).

Results: A total of 27 patients participated in the interviews (17 in the US and 10 in Germany); with 10 patients in the US participating in the app-based task. Patient interviews identified 36 symptoms. Of these, seven primary symptoms were spontaneously reported and considered by participants as among the most frequent, most bothersome or the worst symptoms that they experienced: nasal congestion (n = 27/27, 100%), difficulty breathing (n = 27/27, 100%), post nasal drip (n = 25/27, 92.6%), runny nose (n = 24/27, 88.9%), head/facial pressure (n = 23/27, 85.2%), loss of smell (n = 23/27, 85.2%), and loss of taste (n = 22/27, 81.5%). Symptom experiences were similar for US and German patients. Impacts of NP reported by participants included tiredness/fatigue, blowing their nose, limitations in physical activity, sleep disturbances and impacts on ability to do daily activities. Participants also highlighted the emotional and social impacts of NP. In the app task new symptoms were elicited in addition to confirmation of the majority of symptoms and impacts reported in the interviews. Twenty-four symptoms were reported in both the app task and the interviews, with an additional four symptoms (ear pain, throat pain, nasal scabs and nasal burning), reported only through the app. Considerable day-to-day variability in the severity of symptoms and associated impacts was evident.

Conclusion: Recurrent NP is associated with a wide range of symptoms which can have a significant impact on patients' lives. Findings from the app task, particularly the symptom and HRQoL concepts

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TP1362 | Eosinophilic otitis media in eosinophilic granulomatosis with polyangiitis: A single-center cohort

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Background: Eosinophilic otitis media (EOM) is common but underestimated complication in patients with eosinophilic granulomatosis

with polyangiitis (EGPA). When untreated, patients with EOM show progressive hearing impairment with deterioration of bone conduction. This study aimed to investigate the prevalence and factors associated with EOM in EGPA patients.

Method: EGPA patients diagnosed by the American College of Rheumatology (ACR) criteria between January 1995 and November 2018 were evaluated. Patients were treated with intravenous cyclophosphamide pulse therapy when major organ involvement (heart, gastrointestinal tract, central nervous system or kidney) or neuropathy was present at initial diagnosis. During the regular follow-up after treatment of EGPA, patients with new onset otologic symptoms were evaluated by otoscope and were referred to otolaryngologist for the further evaluation of EOM. Medical records were reviewed to determine factors associated with EOM.

Results: Of 75 EGPA patients (36 males, 39 females), 18 patients (24.0%) were diagnosed as EOM during mean follow-up period of 7.9 years. The most common otologic symptom was otorrhea (42.1%) along with hearing loss (31.6%) and ear fullness (26.3%). Mild to moderate hearing loss was confirmed in 10 patients by audiogram. Two patients (11.1%) showed improvement of symptoms by myringotomy or ventilation tube (VT) insertion only, while 16 patients (88.9%) needed increase of oral corticosteroids dose for symptoms control. High level of blood eosinophil count at initial diagnosis (5570 vs 3429/μL, $P = 0.007$) and higher peak blood eosinophil count after treatment (1580 vs 1472/μL, $P = 0.01$) were associated with development of EOM. Presence of ANCA was very rare in the EOM group (0% vs 18.5%, $P = 0.045$).

Conclusion: EOM is common among EGPA patients even after successful immunosuppressive treatment. Frequent and regular evaluation of otologic symptoms should be taken into account for EGPA patients, especially when initial blood eosinophil level is high.

TP1363 | Diagnostic value of salivary liquefied carbohydrate antigen KL-6 in children with pneumonia

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Background: To investigate the diagnostic value of salivary liquefied carbohydrate antigen KL-6 and the relationship with the severity in children with pneumonia.

Method: A total of 269 children with pneumonia and 112 children with non-pulmonary disease were collected from the First Affiliated Hospital of Guangzhou Medical University. The age of them was under 16 years old. Serum levels of KL-6 were detected.

Results: The serum KL-6 level of pneumonia group was higher than the non-pulmonary disease group [170.0(121.0, 272.0) U/mL vs 119.5(88.3, 156.0) U/mL], the difference had statistically significant($Z = -6.463$, $P < 0.001$). The AUC of the diagnostic test was 0.82 (95% CI: 0.71 to 0.94, $P < 0.001$), The Youden index of 0.506 was selected as the cutoff point. The sensitivity was 65.50%, the specificity was 92.60%, the accuracy rate was 78.57%, the positive predictive value was 90.48%, and the negative predictive value was 71.43%. The Kappa value was 0.58 [0.37, 0.78]. The serum KL-6 level of severe pneumonia group was higher than the mild to moderate pneumonia group[277.0(204.0, 395.0) U/mL vs 163.5(116.0, 248.8)U/mL], the difference had statistically significant($Z = -5.241$, $P < 0.001$). The AUC of diagnostic test was 0.89 (95% CI: 0.81 to 0.96, $P < 0.001$). The Youden index of 0.452 was selected as the cutoff point. The sensitivity was 93.20%, the specificity was 78.00%, the accuracy rate was 85.88%, the positive predictive value was 82.00%, and the negative predictive value was 91.43%. The Kappa value was 0.72 [0.57, 0.86].There was no significant difference of KL-6 level among the children with bacterial pneumonia, mycoplasma pneumonia and viral pneumonia.

Conclusion: The serum KL-6 level has certain clinical application value in the diagnosis of pediatric pneumonia and the prediction of severe pneumonia in children, but there is no specificity between different pathogens induced pneumonia.

TP1364 | Successful intravaginal graded human seminal plasma desensitization in a Can F5 sensitized patient

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Case report: Seminal plasma hypersensitivity presents as local vaginal and/or systemic reactions immediately after contact with seminal fluid. Prostate-specific antigen (PSA) has been identified as one of the causative allergens with an unknown prevalence. There is known cross-reactivity between human PSA and dog allergen Can f 5. Desensitization is an unstandardized treatment for SPH. No previous cases of seminal plasma desensitisation in Can f5 sensitised women have been reported. We present a case of a 34-year-old woman who had ocular itching, facial swelling and difficulty in breathing ten minutes after sexual intercourse. Frequently, she attended A&E requiring IV treatment. She has rhinitis on contact with dust, dogs and horses. Skin prick test (SPT) was performed both to common aeroallergens and to fresh undiluted human seminal fluid. SPT was positive to house dust mites, timothy grass, dog and horse dander. Her blood test showed a Total IgE of 74 IU/mL, seminal fluid IgE < 0.35kUA/L, dog dander IgE 20.1kUA/L, rCan f5 IgE 30.60kUA/L. Determination of serum-specific IgE against dog dander, recombinant Can f 5 and human

seminal plasma was performed using the ImmunoCAP test from Phadia. SPT to fresh undiluted human seminal fluid was positive with a wheal of 6 mm. As she wanted to conceive, human seminal plasma desensitization was proposed. After consent, both patient and partner (the donor) were tested for HIV, hepatitis B and C. Intravaginal graded challenge with human seminal plasma was performed following a previously published protocol. The only alteration was the use of saline solution for the dilutions. Patient was premedicated. The patient tolerated the desensitisation with a starting dosage of 2 mL at a concentration of 1:100 000 and finishing with 2 mL of neat seminal fluid. The procedure had a significant impact on the quality of life of both the patient and her partner. To maintain tolerance, she has been instructed to have unprotected intercourse a minimum of two times per week. Intravaginal graded desensitisation with human seminal plasma is a safe procedure to acquire tolerance to seminal fluid. We present a protocol that could be used in similar cases. A noteworthy difference with previously published cases is the dilution remained stable using a saline solution instead of human albumin as diluent. We raise awareness about the involvement of Can f5 in seminal plasma hypersensitivity, and the relevance of asking about it in dog sensitized patients.

TUESDAY, 4 JUNE 2019
TPS 43
UPDATE ON BIOLOGICALS

TP1365 | The efficacy of omalizumab in severe pruritus associated to immune checkpoint inhibitor: First case report in Spain

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Case Report:

Background: Immune checkpoint inhibitors (anti-PD-1/L1 and anti-CTLA-4) are a new class of cancer therapeutics that promote antitumor immune responses. These medications have reported a 30% of cutaneous toxicity, and the full spectrum of which is not yet completely characterized. We report the first case of the use of omalizumab as a promising option in the pruritus grade 3 toxicity treatment in a patient with pembrolizumab (anti-PD-1) for irresectable melanoma.

Method and Results: A 52-year-old woman diagnosed with irresectable melanoma. She underwent systemic treatment with pembrolizumab (2 mg/kg every 21 days) and definitive radiation therapy, with positive response to the combination. However, after 2 cycles of treatment she developed itching that increased gradually with eczematous eruption that involves thorax, abdomen and upper limbs.

She was initially diagnosed with pruritus grade 2 and treated with antihistamine and topic corticosteroids by her oncologist. After 21 cycles of treatment she developed intense, constant and self care limiting pruritus (Grade 3).

The patient was admitted to Allergy Department and we performed chronic idiopathic urticaria protocol, including skin prick tests with environmental allergens, common foods, mold spores and pet dander that was negative. Complete blood account, biochemistry, PCR, thyroid autoantibodies, serum tryptase, complement levels and stool sample analysis were normal. Total IgE was 122 kU/L.

Systemic corticosteroids and conventional immunosuppressive medications were relatively contraindicated, as they could interfere with the intended antitumor activity of Pembrolizumab. For that, we started Omalizumab as recommended in NCCN guidelines to the management of immunotherapy-related toxicities if elevated IgE.

The patient impaired a rapid response achieving a complete resolution. At the time of submission, the patient remains without cutaneous symptoms since the first dose of Omalizumab.

Conclusion: Possible pathogenesis of pruritus remains unclear in this group of patients, but xerosis and skin inflammation due to mast cells and basophils degranulation have been proposed. The combination among immunotherapies for cancer is increasing, and Omalizumab is a promising option for management of cutaneous toxicity avoiding the use of systemic corticosteroids. Additional studies are needed to further evaluate these promising results.

TP1366 | Importance of skin tests in the evaluation of hypersensitivity reactions to monoclonal antibodies

Jimenez-Rodriguez TW[1,2]; Colomer-Aguilar C[3]; Ruano-Zaragoza M[1,2]; Soriano-Gomis V[1,4]; Gonzalez-Delgado MP[1,4]; Fernandez-Sanchez FJ[1,4]

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Background: Increased use of Monoclonal Antibodies (MAb) has led to an increase in Hypersensitivity Reactions (HSRs), which constrain their use. Skin tests have been used to diagnose reactions with these agents. A series of patients with HSRs to different MAb at the University General Hospital of Alicante in the period March-December 2018 were studied.

Method: Eight patients developed Immediate HSRs: 4 (50%) to rituximab, 1 to infliximab, 1 to adalimumab, 1 to bevacizumab and 1 to nivolumab. HSRs severity was graded by the modified Brown classification, in accordance with this, 5 (62.5%) patients presented reactions grade II; 2 reactions grade III, and 1 reaction grade I. Seventy five percent of patients, that is 6, had clinical reactions suggestive of the cytokine release phenotype, 1 of phenotype I, and another one of mixed phenotype.

Skin tests were performed with the MAb involved in the reaction, provided by the Hospital Pharmacy Service in sterile dilutions at the concentrations recommended in previous publications.

Results: Only 1 (12.5%) patient, the only one with phenotype 1, had positive skin tests with adalimumab (intradermal test concentration 1/1000) and a Basotest that was also positive at the same MAb. The rest of the patients studied (7 = 87.5%) had negative skin tests.

Conclusion: Skin tests may be useful due to the positive correlation with clinical manifestations, thus allowing the identification of patients with IgE-mediated reactions, and offering them the appropriate therapeutic alternatives, including desensitization or pretreatment in future exposures.

TP1367 | Assessment and prediction of cetuximab-induced hypersensitivity reactions using specific IgE detection

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Background: Cetuximab, a chimeric mouse-human IgG1 monoclonal antibody against the epidermal growth factor receptor, has proven effective in the treatment of metastatic colorectal cancer and squamous cell carcinoma of the head and neck. It is known that cetuximab can induce hypersensitivity reactions (HSR) even at the first administration due to cross-reactivity with galactose alpha-1, 3-galactose (alpha-gal). We aimed to find a precise screening method to predict cetuximab-induced HSR.

Method: Patients over 18 years of age who scheduled for cetuximab administration according to standard treatment guidelines were enrolled prospectively. Before first cetuximab administration, specific IgE to cetuximab, alpha-gal and beef were measured using ImmunoCAP. Skin prick test (SPT) was done with cetuximab. Adverse drug reactions were monitored after cetuximab administration.

Results: Among the 63 patients who participated in this study 3 patients (4.8%) experienced HSR (anaphylaxis). Median level of cetuximab specific IgE was 9.96 kU_A/L (range: 4.13-36.40 kU_A/L) in HSR group and 0.00 kU_A/L (range: 0-0.18 kU_A/L) in the control group (*P* value < 0.001). Among the 3 anaphylactic patients, two patients performed SPT and it showed positive reactions. The results of alpha-gal and beef sIgE were similar to those of cetuximab sIgE. Patients who did not experience HSR were all negative in 4 tests. Therefore, sIgE detection of cetuximab, alpha-gal, and beef by ImmunoCAP showed 100% of sensitivity, specificity, positive predictive value and negative predictive value.

Conclusion: Specific IgE detection of cetuximab and its cross-reactive allergen using ImmunoCAP and SPT can predict cetuximab-induced anaphylaxis before first administration.

TP1368 | IL-5-modulating agents are an effective novel therapy for severe and life-threatening eosinophilic disorders

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Background: The clinical spectrum of eosinophilic diseases is broad and many of these conditions can be life threatening. Currently, limited therapeutic options are available. Interleukin (IL)-5 is a key mediator of eosinophilic inflammation. However, data regarding the use of IL5-modulating agents in eosinophilic disorders, other than eosinophilic asthma, are scarce.

Method: A retrospective analysis of medical records of patients, who were admitted to Hadassah-Hebrew University Medical Center, Jerusalem, Israel, during the period of 2003-2018, and treated off-label using IL-5-modulating agents, was performed.

A retrospective analysis of medical records of patients, who were admitted to Hadassah-Hebrew University Medical Center, Jerusalem, Israel, during the period of 2003-2018, and treated off-label using IL-5-modulating agents, was performed.

Results: We identified 8 patients with a mean current age of 50.5 (range: 17-66) years. Diagnoses included primary hyper-eosinophilic syndrome, eosinophilic granulomatosis with polyangiitis (EGPA), asthma treated with a combination of omalizumab and benralizumab, eosinophilic cellulitis (EC; Wells syndrome) and eosinophilic fasciitis (EF; Shulman's syndrome). Respiratory, skin, gastrointestinal and cardiac manifestations were noted in 6, 6, 1 and 2 patients, respectively. The clinical manifestations of these eosinophilic disorders were severe and refractory to treatment with other glucocorticoid-sparing medications. Mean peak eosinophil count and C-reactive protein (CRP) were 10.36 (2.4-17.1) cells x 10^9/L and 25.5 (5.6-99.9) mg/dL. Mepolizumab was given to 5 patients [HES, EC, EGPA and EF (100 mg every 4 weeks) and EGPA (300 mg every 4 weeks)]. Three other patients (2 EGPA and one asthma) were treated with benralizumab (30 mg every 8 weeks). All patients clinically improved following treatment. Complete resolution of symptoms was noted in 4 patients. In addition, glucocorticosteroids were discontinued in 6 patients and cyclophosphamide in 2 patients. Mean eosinophil count and CRP decreased to 0.09 (0-0.36) cells x 10^9/L and 1.54 (0.06-7.46) mg/dL, respectively.

Conclusion: IL-5-modulating agents may be effective in severe and life-threatening eosinophilic disorders. Their routine use in refractory diseases should be further explored.

TP1369 | Three specific monoclonal antibodies bound to the major birch allergen Bet V 1 are sufficient to block IgE-mediated allergic response

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Background: Allergen-induced crosslinking of IgE bound to Fc-epsilon receptors on effector cells triggers the allergic cascade. A cocktail of two allergen specific IgG monoclonal antibodies (mAbs) is effective in blocking allergen binding to IgE and preventing an allergic response to Fel d 1, the major cat allergen (Orengo, 2018). Using

a similar approach herein we describe the structural characterization of three mAbs bound to Bet v 1 and demonstrate that this cocktail is sufficient to prevent Bet v 1 binding to polyclonal IgE.

Method: Bet v 1 specific mAbs, REGN5713, REGN5714 and REGN5715, were isolated from Regeneron's VelocImmune human antibody mouse platform. Binding kinetics and sequential binding competition were determined using surface plasmon resonance. An ELISA using IgE from birch allergic individuals assessed the ability of REGN5713, REGN5714 and REGN5715 to block IgE binding to Bet v 1. X-ray crystal structures of the REGN5713 and REGN5715 Fab fragments bound to Bet v 1 were determined. Electron microscopy (EM) of Bet v 1 bound to REGN5713 + REGN5714 + REGN5715 Fabs revealed the three-dimensional architecture of the complete complex.

Results: REGN5713, REGN5714, and REGN5715 simultaneously bindBet v 1 with high affinity and non-competitively. A triple combination of REGN5713-5714-5715 was most effective in blocking Bet v 1 binding to polyclonal IgE derived from 16 different birch allergic subjects; double and single antibody combinations showed lower blocking levels across all samples. Crystal structures of the complex of Bet v 1 with Fabs of either REGN5713 or REGN5715 show that the heavy and light chain of REGN5713 interact extensively with a broad flat surface of Bet v 1, whereas REGN5715 interacts with a small contiguous epitope through heavy chain contacts only. Negative stain EM reveals a planar and roughly symmetrical complex formed by REGN5713 + REGN5714 + REGN5715 bound to Bet v 1; this complex geometry is consistent with the crystal structure data.

Conclusion: REGN5713, REGN5714 and REGN5715 bind non-competitively to Bet v 1 with high affinity and effectively block Bet v 1 binding to polyclonal IgE. Structural data show that simultaneous binding of REGN5713 and REGN5715 leaves more than half of the surface area of Bet v 1 exposed. REGN5714 binds in the exposed region, but cannot cover all of it, suggesting that it is not necessary to mask 100% of the allergen surface with an antibody cocktail in order to achieve maximal blocking potency.

TP1370 | Management problems in severe chronic inducible urticaria: 2 case reports

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Background: Chronic inducible urticaria (CIndU) is a subgroup of chronic urticaria which can cause severe quality of life impairment by their refractory forms. The recommended treatment approach in CindU is the same as that for chronic spontaneous urticaria (CSU). However, CIndU seem to be more resistant to standard doses of H1 antihistamines (AHs) and higher doses of AHs are required for symptom control. Omalizumab, a recombinant anti-IgE antibody, effectively treats CSU. Nevertheless, there is not enough evidence in patients with CIndU, especially in AHs resistant cases.

Method: We describe 2 patients with 2 subtypes of CIndU: one with severe cold urticaria (including anaphylaxis) and the other with severe extensive symptomatic dermographism. In both cases, we have performed complete positive and differential diagnostic work-up. Management strategies included first line and second line symptomatic therapy, but with no success in both cases. Avoidance of eliciting triggers was difficult to achieve (occupational reasons). We decided to start omalizumab treatment, 300 mg every 4 weeks for 6 months.

Results: The cold urticaria patient gained complete symptom relief 10 days after the first dose of omalizumab; the quality of life improved substantially with no side effects of the treatment. The urticaria factitia patient showed no benefit of the add-on 5 months treatment with omalizumab. He refused the sixth dose of omalizumab due to the lack of response, and also cyclosporine, but he showed some benefits of oral corticosteroids.

Conclusion: Although many clinical studies support the use of omalizumab in the treatment of patients with CIndU, we certainly need more data for prediction of a good clinical response.

TP1371 | Efficacy of omalizumab in hereditary alpha tryptasaemia

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Case Report: Hereditary alpha-tryptasaemia is a recently described disorder associated with elevated basal serum mast cell tryptase concentrations due to increased copy numbers in the tryptase alpha/beta1 (*TPSAB1*) gene. Clinically, it presents with multiorgan symptoms.

We describe a 56-years old woman with longstanding chronic urticaria (predominant), dermographism (confirmed by a challenge testing with a calibrated dermographometer with the reaction to the lowest pressure of 20 g/mm^2), skin flushing, food intolerances and abdominal bloating, allergic asthma, rhinosinusitis, odynodysphagia and globus sensation. Her daughter apparently suffers from “sensitive and very itchy skin”. The patient's symptoms had become worse over the last few years and were exacerbated by stress. UAS7 score was persistently elevated (28-33). Baseline serum mast cell tryptase fluctuated between 15 - 22 ng/mL. Blood eosinophil count was normal. Total IgE was raised (500 kIU/L), with specific IgE positive to house dust mite, grass pollen and cat

dander. Basophil histamine release assay was negative (0%). Skin biopsy showed an infiltrate of CD117 + mast cells with perivascular distribution in the dermis and considered non-diagnostic. *KIT* mutation screen and bone marrow were normal. *TPSAB1* copy number analysis by droplet digital PCR (ddPCR) identified an allele duplication, resulting in a total of three copies of the alpha-tryptase encoding sequence in *TPSAB1*.

Skin symptoms were not controlled with high dose antihistamine and montelukast and she only had a transient response to short courses of oral prednisolone 0.5 mg/kg. However, monthly SC omalizumab 300 mg led to symptomatic benefit following the first dose (after 48 h) and UAS7 score of 0, as well as improved asthma control.

In conclusion, we describe a patient with hereditary alpha-tryptasaemia with a confirmed *TPSAB1* allelic duplication and debilitating recalcitrant chronic urticaria, who showed marked improvement with omalizumab. Larger clinical series are required to establish efficacy of omalizumab in this condition.

TP1372 | Efficacy and safety of omalizumab for severe Japanese cedar pollinosis in patients treated with combination oral antihistamines and nasal corticosteroids

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Background: Japanese cedar pollinosis (JCP) is the major cause of seasonal allergic rhinitis (AR) in Japan with 30% nationwide prevalence. Due to excessive pollen dispersal, 25% of JCP patients have continued symptoms despite standard treatments including oral antihistamines and nasal corticosteroids. Efficacy of omalizumab (anti-IgE) added to the standard treatment regimen was evaluated for severe JCP.

Method: Adolescent and adult patients with severe JCP in Tokyo and surrounding areas were enrolled in a 12-week double blinded, placebo controlled, randomized parallel treatment study conducted during the 2018 pollen season. Patients were randomized in a 1:1 ratio to receive omalizumab or placebo added to standard treatment regimen according to the dosing table. The primary endpoint was mean nasal symptom score (within the severe symptom period). Additional endpoints included mean ocular symptom score, medication score, Japanese Rhinoconjunctivitis Quality of Life Questionnaire (JRQLQ), Work Productivity and Activity Impairment Questionnaire-Allergy Specific (WPAI-AS), and nasal symptom free days.

Results: 336 Japanese patients received either omalizumab (n = 161) or placebo (n = 175), and approximately 98% completed the treatment period. Baseline characteristics were similar between treatment arms. Differences in LS means for nasal and ocular symptom scores between omalizumab and placebo arms were clinically relevant with −1.03 (95% confidence interval [CI]: −1.44 to −0.62, $P < 0.001$) and −0.87 (95% CI: −1.18 to −0.55, $P < 0.001$), respectively. Omalizumab reduced mean nasal and ocular symptom medication scores with LS mean differences of −1.10 and −0.95, respectively. JRQLQ scores and WPAI-AS scores (impaired percentages) across all domains improved for patients receiving omalizumab versus placebo. Omalizumab enhanced work productivity and activity scores (95% CI), by LS mean differences of −13.61 (−20.09, −7.13) and −14.16 (−19.90, −8.42), respectively. The median number of nasal symptom free days during the 30-day severe symptom period was higher in omalizumab arm (15.0 days) than in placebo arm (10.0 days). No unexpected safety signals were identified.

Conclusion: In patients with severe JCP, omalizumab reduced symptoms and improved quality of life and productivity outcomes compared with placebo. Findings indicate that omalizumab therapy has potential to improve the management of severe AR, representing an advance from both patient and societal perspectives.

TP1373 | Effect of omalizumab in peripheral T cell subpopulations in chronic urticaria

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Background: Chronic urticaria (CU) is an spontaneous urticaria that lasts for at least 6 weeks without an allergic trigger. In 40% of the patients an autoimmune pathogenesis, IgE-mediated, is involved. Severity and prognosis are highly variable among patients, and therapeutic management needs to be personalized. Omalizumab, a IgG1k monoclonal antibody that binds free human immunoglobulin E (IgE) has shown therapeutic effect in some patients.

Objective: To analyze the effect of Omalizumab in peripheral blood T-cell subpopulations of CU patients.

Method: Naïve, central memory, effector memory, effector (Th1, Th2, Th17)T-cell subpopulations and activation markers (CD38, HLA.DR) were analyzed in peripheral blood (PB) of 49 CU patients (Omalizumab treatment (n = 22); non immunomodulatory drugs (n = 27)) and 50 healthy donors (HD).

Results: Compared to HD, CU patients in treatment with non-immunomodulatory drugs showed lower percentages of $CD4^+$ DR^+ $CD38^+$ [0.8(0.7-1) vs 1.23 (1.01-1.54), $P < 0.0001$] and $CD4^+$ DR^+ $CD38^-$ [1.1 (0.8-1.4) vs 3.07 (2.5-4.7), $P < 0.0001$]. Percentages of $CD8^+DR^-CD38^+$ [21 ± 3 vs 8 ± 0.5%, $P < 0.0001$] and $CD4^+$ naïve [55 ± 3 vs 41 ± 2, $P < 0.0001$] subpopulations were increased.

CU patients in treatment with Omalizumab, showed lower percentage of $CD4^+HLA\text{-}DR^+CD38^+$ [0.75(0.6-1.1) vs 1.23(1.01-1.54)%,

$P < 0.0001$],$CD4^+DR^+CD38^-$ [1.7(0.7-3.15) vs 3.07(2.5-4.7)%, $P = 0.0006$] and higher percentage of $CD8^+DR^-CD38^+$ [14 ± 2 vs 8 ± 0.5%, $P = 0.0001$] and Th1 Central-Memory cells [12 ± 0.8 vs 9 ± 0.4%, $P < 0.0001$] than HD. Patients under Omalizumab showed a decrease in $CD4^+$ naïve [42 ± 3 vs 55 ± 3%; $P = 0.001$] and $CD4^+DR^-CD38^+$ [36 ± 3 vs 52 ± 3, $P = 0.0002$] compared to patients under non-immunomodulatory drugs.

Th1CM [12 ± 1 vs 9 ± 1, $P = 0.013$], Effector Memory [5.7(4.6-10.2) vs 4.2 (3.6-6.8))%, $P = 0.033$] and Th2 CM[8.5 (6.7-12.3) vs 6.4(4.3-8))%, $P = 0.019$] cells were increased in Omalizumab patients.

Conclusion: Omalizumab induces changes in peripheral blood T-cell subpopulations of CU treated patients, promoting a decrease of activated T subsets, and an increase of effector Th1 and Th2 cells. The impact of these changes on treatment response deserves further investigation.

TP1374 | A real life experience of omalizumab: Nine-year follow-up of 205 patients in a single center

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Background: Omalizumab is licensed for the treatment of severe allergic asthma and chronic urticaria. However, real-life data are needed for long term use.

Aim: We aimed to evaluate all of our patients' demographics, clinical characteristics as well as conditions observed during the follow-up period of omalizumab prescribed for different indications in the last 9 years.

Method: Demographic and clinical data of 205 patients followed in our adult allergy clinic who were treated with omalizumab between August 2009 and December 2018 were retrospectively reviewed. Asthma Control Test (ACT) and seven-day Urticaria Activity Score (UAS7) were used to assess the level of symptom control at the initial and follow up visits in asthma and chronic urticarial patients, respectively.

Results: The mean age was 42.40 ± 12.46 years and 73.2% of the patients were female. The clinical and demographic characteristics of the patients were summarized in Table-1. Before omalizumab treatment, ACT scores were < 19 in 55 and 20-24 in 4 asthma patients and after 16 weeks of omalizumab treatment ACT scores were 25, 20-24 and < 19 in 44, 13 and 2 asthma patients, respectively. Before omalizumab treatment, UAS7 scores were 28-47 and 16-27 in 122 and 4 chronic urticaria patients, respectively. With omalizumab treatment, UAS7 scores significantly reduced in 2/3 of the patients. During omalizumab treatment, the clinical conditions that were observed were as follows: thrombocytopenia in 1 patient, pancreatic cancer in 1 patient, endometrial cancer in 1 patient, exacerbation of urticaria plaques in 2 patients and pregnancy in 1 patient. During pregnancy, omalizumab was continued without any trouble. In the follow-up of 14 chronic urticaria patients dose intervals were increased to 45 days and in 2 of them symptoms relapsed. Two patients benefited from 150 mg omalizumab in every 2 weeks. In 6 patients, omalizumab dose was increased to 450 mg monthly. In 2 patients, cyclosporine was added to omalizumab.

Features	n: 205	%
Gender		
Female	150	73.2
Male	55	26.8
Diagnosis		
Severe asthma	59	29.2
Chronic urticaria	127	61.5
ABPA	5	2.4
Idiopathic histaminergic angioedema	10	4.9
Idiopathic anaphylaxis	4	2
Conditions developed during treatment		
Thrombocytopenia	1	0.5
Endometrial cancer	1	0.5
Pancreatic cancer	1	0.5
Exacerbation of urticaria	2	1
Pregnancy	1	0.5
Autoimmunity		
Yes	38	18.5
No	156	76.1
Missing data	11	5.4
Omalizumab discontinuation		
Yes	74	36.1
No	131	63.9
Recurrence after discontinuation		
Yes	35	17.1
No	170	82.9
	Min – Max	Mean±SD
Age (years)	18-76	42.40 ± 12.46
Body Weight (kg)	43-110	71.55 ± 12.75
Omalizumab monthly dose (mg)	150-1200	337.31 ± 199.21
	Min – Max	Median
Duration of treatment (months)	2-111	12
Eosinophil count (mm^3)	0-1500	120
Total IgE (U/L)	3-4480	166

Conclusion: Omalizumab is an effective and a safe biological agent for severe allergic asthma and chronic resistant urticaria. Omalizumab treatment should be personalized in the context of doses, intervals between doses and continuity in the patients with chronic urticaria.

TP1376 | Anti-eosinophil therapy is associated with decreased body mass index in severe asthmatics: A retrospective analysis

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Emory University School of Medicine, Atlanta, United States

Background: The type 2 high endotype of asthma with adult onset symptoms is often characterized by severe persistent, steroid refractory eosinophilic inflammation. The amelioration of eosinophilic inflammation through anti-IL-5 therapies reduces exacerbations and improves asthma control in this setting. Anti-IL-5 agents have a glucocorticoid sparing effect in severe eosinophilic asthma and are overall well tolerated. However, an accumulating body of evidence implicates a role for eosinophils in adipose tissue (AT) homeostasis and weight loss. The effect of anti-IL-5 mediated eosinophil depletion on patient weight is hitherto unknown.

Method: We sought to examine the impact of long-term therapy with anti-eosinophil agents on body mass index (BMI) in subjects with severe asthma. Electronic medical records were searched for patients with severe adult onset asthma treated with anti-IL5 agents between January 2016 and September 2018 at a single tertiary care center. Six-month clinical and laboratory data were retrospectively collected by chart review.

Results: 51 patients (29.7% males, mean age 56.7 ± 13.4 years) met inclusion criteria, of whom 23 had BMI > 30. 19 (37.2%) subjects were on maintenance oral corticosteroids at baseline. During the 6-month follow up period, there was no significant weight gain observed in the cohort as a whole, nor when stratified by BMI or by the anti-IL-5 agent used. Mean BMI amongst the cohort decreased by 1 point ($P = 0.03$) and was similar across anti-IL5 agent used. This effect appeared especially pronounced in the subset of obese patients with baseline BMI > 30, with a mean BMI decrease of 2.3 across all of the anti-IL-5 agents, which was significant compared to the remainder of the cohort ($P = 0.04$).

Conclusion: Anti-IL5 therapies were associated with weight loss in a cohort of severe asthmatics during six-month follow up. Given the epidemic increase in incidence of asthma as well as obesity in recent decades, these findings need validation in larger studies. Future studies are also warranted to elucidate the role of eosinophils in AT homeostasis and obese asthmatics in order to optimize precision treatments.

TP1377 | Patients with severe eosinophilic asthma treated with mepolizumab: A 12-month follow-up from our clinical practice

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Background: Mepolizumab, a humanized anti-interleukin-5 antibody, has been shown to reduce the rate of exacerbations and to improve several clinical endpoints in patients with severe eosinophilic asthma (SEA).

Method: We performed a descriptive, retrospective study. Patients with uncontrolled SEA treated with mepolizumab followed up in the severe asthma unit from Hospital La Paz were included. We entered demographic data, clinical characteristics and management of these patients in a national registry. These data were collected before initiating mepolizumab therapy, at a follow-up visit performed 4-6 months later, and after 12 months of treatment. Ethical committee approval was obtained(PI-3325).

Results: Sixteen patients were included (median age 53.8 ± 16.5 years old), 62.5% were female. Eight patients (50%) had allergic asthma. All patients were on GINA step-5 therapy. Ten patients (62.5%) had previously received omalizumab.

After 4-6 months of treatment, the rate of exacerbations was reduced by 91% (total exacerbations in the 12 months before mepolizumab: 44 vs after 4-6 months: 4)($P < 0.001$). The mean increase from baseline in forced expiratory volume in 1 second (FEV_1) was 185 mL ($P = 0.098$). Peripheral eosinophilia was reduced by 81% after 4-6 months ($P < 0.001$). Improvement in ACT score from baseline (19 ± 4) vs first follow-up visit (21.4 ± 2.8) was 4.7 points ($P = 0.002$). Until now, data of 8/16 patients could be obtained after 12 months of treatment. The rate of exacerbations was reduced by 96.3% (total exacerbations in the 12 months before mepolizumab 44 vs 1 after 12 months) ($P = 0.005$). After treatment, no significant differences were found in FEV_1 ($P = 0.9$). Peripheral eosinophilia was reduced by 91% after a year of treatment ($P < 0.001$). No significant improvement in ACT score from baseline (19 ± 4) vs last follow-up visit (21 ± 5) was observed, as well as in results of fractional exhaled nitric oxide (FeNO): 106 ± 89 vs 90 ± 43 ($P = 0.6$).

Mepolizumab was stopped after an adverse event in one patient.

Conclusion: Mepolizumab in our clinical practice improved asthma control, with a significant reduction in peripheral blood eosinophilia and the number of asthma exacerbations after 4-6 months of treatment. In the following 6 months, the patients maintained an almost inexistent rate of exacerbations, low levels of blood eosinophils and FeNO with respect to their initial values.

TP1378 | Mepolizumab - a reference center experience

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Background: In the treatment of severe asthma, besides the optimized inhaled therapy, the need of daily systemic corticotherapy is frequent. The regular use of corticosteroids can result in serious adverse effects, which sometimes are irreversible. Mepolizumab is a humanized monoclonal antibody that blocks IL-5 (an eosinophilic inflammation mediator) and which has shown to reduce the number of exacerbations in patients with severe eosinophilic asthma, when used as an additional treatment.

Method: We analyzed the clinical records of 18 patients under Mepolizumab at our Department. We included only those who were under treatment at more than 6 months; therefore, 8 patients were excluded. All of them did 100 mg Mepolizumab from 4/4 weeks. It was analyzed the demographic data, clinical presentation, eosinophil count at peripheral blood, pulmonary function, usual and relief medication and asthma control through the Asthma Control Test (ACT), before and after the treatment.

Results: There were included 10 patients, with an average age of 59 ± 9, 7 were women. All had allergic rhinitis and were medicated with an antihistamine and an ICS+LABA. Only one patient wasn't medicated with montelukast. Three patients had already done Omalizumab, without clinical improvement. Based on ACT, before treatment start, all patients had uncontrolled asthma (ACT > 20). After 6 months, 5 patients already presented partly controlled asthma (ACT 20-24). It was verified a significant decrease (average of less 82.9%) in the number of peripheral blood eosinophil count. Of the 4 patients who did pulmonary function tests at 6 months of therapy, FEV1 remained overlapping in 3 patients and increased 24% in 1 patient. After 6 months, 4 of the 5 patients who were under daily systemic corticosteroids have reduced the intake to alternate days. In the remaining patients who did frequent cycles, there was a decrease in the need of corticosteroids as well as in the number of exacerbations. Regarding the adverse effects, there was only reference to 2 cases of myalgias, which reverted with magnesium.

Conclusion: Mepolizumab was well tolerated in the majority of the patients, with a good safety profile. There was a decrease in corticosteroid dependence as well as in the number of exacerbations in all of the patients.

TP1379 | Ophthalmological characteristics and treatment outcomes of conjunctivitis in patients receiving dupilumab for moderate-to-severe atopic dermatitis

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Background: Daily clinical practice observations using dupilumab indicate an unanticipated high incidence of conjunctivitis as a treatment-related adverse event. Few studies have been published on conjunctivitis during dupilumab treatment, which are limited by their retrospective design, small sample sizes and lack of ophthalmologist-confirmed cases. This study evaluated ophthalmological characteristics and treatment outcomes of conjunctivitis occurring during dupilumab.

Method: In the prospective Bioday Registry we identified all ophthalmologist-diagnosed cases of conjunctivitis occurring in AD patients that received dupilumab according to label between January and December 2018 at the University Medical Center Utrecht, Utrecht, The Netherlands. All patients underwent a standardized ophthalmologic assessment and follow-up including, grading of severity (mild, moderate or severe) and prescribed medication for the treatment of conjunctivitis.

Results: In total, 33 patients were included of which 23 (70%) had a history of allergic conjunctivitis. At baseline, 2 patients reported sicca complaints and 4 patients had active allergic (kerato)conjunctivitis. Median follow-up duration was 8.6 months (IQR 7-12 months); median interval between starting dupilumab and conjunctivitis diagnosis was 3.2 months. Patients who primarily presented with moderate-to-severe conjunctivitis (n = 20, 61%) had a significantly higher tendency to develop persistent conjunctivitis (i.e., having active conjunctivitis at most recent follow-up) (P = 0.005). There were no significant differences between treatment duration or baseline AD severity among mild or moderate-to-severe conjunctivitis patients. Multiple treatments for conjunctivitis were necessary in 22 (64%) cases and included ocular corticosteroids and tacrolimus ointment. A majority (n = 28, 88%) remained medication dependent at their most recent follow-up, of which 20 (61%) still had active conjunctivitis despite adequate treatment. In 11 (33%) cases, dose tapering (n = 9) or treatment discontinuation (n = 2) of dupilumab was required.

Conclusion: In this large case series of ophthalmologist-confirmed conjunctivitis during dupilumab treatment, the majority of patients required chronic use of multiple ocular anti-inflammatory treatments. The severity at initial clinical presentation was significantly related to the persistence of conjunctivitis, but not associated with the severity of AD at baseline, the treatment duration of dupilumab or a history of conjunctivitis.

TP1380 | In atopic dermatitis patients, dupilumab therapy reveals that IgE against food allergens decrease faster than IgE specific for respiratory allergens

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Background: Dupilumab is a therapeutic human monoclonal IgG_4 and an antagonist of the IL-4/13 pathways. In patients treated by dupilumab, the IL-4 dependent Th2 immune response and the mechanisms of IgE production are impaired.

Method: We analysed 27 adult patients (mean 39 y.o., SR 2.4) with moderate/severe atopic dermatitis (AD), by ImmunoCAP™ ISAC (Thermo Fisher Scientific), before debut of dupilumab therapy (bimonthly injections) and then after an average of 127 days of treatment (47-251 days). Specific IgE (sIgE) levels in ISU-E were used to calculate 745 after/before dupilumab ratios of sIgE, with a number of ratios varying from 3 to 77 among patients. Specific IgE < 0.3 ISU-E and ratios < 0.75 were removed from analysis. In addition of ISAC, 3 patients were studied with the ALEX biochip (Macro Array Diagnostics). To compensate for different lengths of dupilumab therapy, we also calculated the half-life for each anti-component sIgE. Total IgE levels were measured by ImmunoCAP.

Results: The average decrease for total IgE in all patients was of 44% (1 to 84%). For sIgE, after/before dupilumab ratios were significantly lower for food-derived components (FD) than for components derived from respiratory allergens (RD) ($P < 0.0001$; Mann-Whitney test). This result was confirmed by testing 3 patients (after/before dupilumab; 65 FD and 82 RD comparisons) with the ALEX biochip ($P = 0.01$). There was no significant difference between glycosylated vs non-glycosylated components, and ratios for cross-reactive components (PR-10, LTPs and profilins) were not different than for other components. After conversion of ratios into half-life of IgE, sIgE directed against FD components have a significantly shorter half-life compared to sIgE specific for RD components ($P < 0.0001$).

Conclusion: In patients treated with dupilumab, blockade of the IL-4/13 pathways blocks the generation of new IgE-producing plasma cells (PC), and "old", pre-existing PC are eliminated at variable rates. Our results demonstrate that in patients with AD, PC producing IgE against FD allergens disappear faster than PC synthesizing IgE specific for RD allergens. This could be due to distinct ways of sensitization (i.e. through altered skin for FD allergens, and through airways for RD), and/or to intrinsic properties of allergens (e.g. lipophilic vs hydrophilic). The rapid decrease of sIgE against FD allergens could also be related to their production by short half-life PC, located outside of the bone marrow.

TP1381 | Cell-penetrating peptide dendrimers as multifunctional therapeutic agents

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Background: Peptide dendrimers (PDs) are hyperbranched oligomers with tree-like structure based on non-natural ε-amide bonds of lysine core. The design of PD constructs with cationic surface clusters promotes their interaction with cell membranes, negative-charged pharmaceuticals and specific extra- and intracellular biological targets. It expands the range of practical applications of PDs, including intracellular delivery of nucleic acids [1], suppression of the tumor growth [2] and various infections. One of the proposed mechanisms underlying their activity is an interaction with multifunctional protein nucleolin (C23). N-terminal part of C23 is highly phosphorylated and contains negatively charged regions rich of glutamic and aspartic acids contributing to bonding with positive PDs. Moreover, the nucleolin has been recently discovered as RSV cellular receptor that is susceptible to a virus F protein. Therefore, the main objective of this work is to develop peptide dendrimers as potential ligands for nucleolin with potential anti-RSV activity.

Method: The peptides were designed taking into account the 3D structure of the Asp/Glu-enriched C23 domains as potential targets and their possibility to prevent the formation of a 6-helix barrel of F protein, i.e. suppress the active-fusion viral state. Novel 12 PDs with different molecular mass, charge and lipophilicity have been synthesized by solid phase method using the Fmoc-protective strategy and their structures were confirmed by HPLC and MALDI-MS. The cytotoxic and antiviral properties have been investigated using RSV-susceptible MA-104 cell line and HeLa as control. Additionally, PDs affinity for nucleolin has been approved their colocalization by confocal microscopy using Cy5-labelled peptides and commercial Ab.

Results: Some of PDs have possessed enough high level of cytotoxicity due to positive net charge and cell membrane penetration; nevertheless the experiments have revealed advantages of dendrimer structure in terms of biocompatibility and antiviral activity in comparison with linear known peptides.

Conclusion: Hits of them have ability to decrease virus titre more than 100 times, which will be tested in biological models in vivo.

Acknowledgments: This work was supported by RSF № 18-74-10002.

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[2] Lushnikova, A. A., et al. *ALLERGY*, 2018, 73, 488-488.

TP1382 | An example of brilliant response to anti TNF treatment in refractory cardiac sarcoidosis

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Case report: A 53 year-old man was referred to our clinic with a diagnosis of sarcoidosis based on trans-bronchial lymph-node biopsy, with documented lung and heart involvement. A previous echocardiography had described a biventricular concentric hypertrophic cardiomyopathy, so he had undergone a cardiac MRI which had demonstrated cicatricial outcomes. He was treated with high dose steroid therapy obtaining clinical stability. After six years an echocardiography showed a dilated hypokinetic heart disease with moderately reduced ejection fraction (EF 40%) and a new Holter ECG described potentially malignant ventricular arrhythmias: for this reason a monocameral ICD was placed in primary prevention and therapy with azathioprine was started. After a period of partial clinical and instrumental improvement, due to the presence of new areas of metabolite uptake at PET-CT, we decided to turn the immunosuppressive therapy on methotrexate. This approach did not meet expectations because the ventricular function decreased again. For this reason anti-TNF therapy was undertook, with brilliant improvement of cardiac function (EF from 35% to 60% before third infusion of Infliximab). This therapy is so far well-tolerated and has allowed progressive steroid tapering.

In conclusion cardiac involvement is a rare and potentially life-threatening complication of sarcoidosis. Anti TNF drugs may be considered as an alternative safe therapeutical option in sarcoidosis with refractory cardiac involvement.

TUESDAY, 4 JUNE 2019
TPS 44
EPIDEMIOLOGY AND RISK FACTORS

TP1384 | International severe asthma registry (ISAR): Mission statement

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Background: Regional/national severe asthma registries provide valuable country-specific information. However, they may be limited by having insufficient statistical power to answer many research questions, lack intra-operability and have fundamental differences in data collected, making cross comparisons difficult. A worldwide registry, which brings all severe asthma data together in a cohesive way, under one umbrella, permitting seamless sharing of data may increase our ability to understand severe asthma.

Method: The International Severe Asthma Registry (ISAR; http://isaregistries.org/) is a multi-country, multicentre, observational initiative. It retrospectively and prospectively collects data on severe asthma patients from pre-existing and new registries (that it helps to set up). It includes patients (≥18 years) receiving care (GINA Step 5 or uncontrolled on Step 4) at severe asthma secondary and tertiary care centres. ISAR aims to improve the care of adults with severe asthma globally (both in primary and secondary care). This aim will be realised by ISAR's key attributes as outlined here.

Results: ISAR is the first global severe asthma registry; a joint initiative where national registries retain ownership of their own data and open their borders and share data with ISAR for ethically-approved research purposes. Its strength comes from collection of patient-level, anonymous, longitudinal, real-life, standardized, high-quality data (using a core set of variables agreed by Delphi consensus) from countries across the world, combined with organizational structure, inclusivity/openness and clinical, academic and database expertise. This gives ISAR sufficient statistical power to answer important research questions, sufficient data standardization to compare across countries/regions and the structure and expertise necessary to ensure its continuance, scientific integrity and the clinical applicability of its research.

Conclusion: ISAR offers a unique opportunity to implement existing knowledge, generate new knowledge and identify the unknown, so promoting new research. With its ability to capture data on a much broader range of severe asthma patients, to compare between registries and robustly assess the impact of therapeutic interventions, ISAR has the potential to become an important platform for the study and better understanding of severe asthma, supporting the appropriate use, and monitoring the impact, of novel asthma therapies.

This abstract is written on behalf of the ISAR Working Group.

TP1385 | Heterogeneity of childhood asthma in Korea: Cluster analysis of children with asthma from Korean childhood asthma study (KAS)

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Background: Asthma is a heterogeneous airway disease with various clinical phenotypes in children. It is important to clearly identify clinical phenotypes to achieve better asthma management and to predict the prognosis. Investigating the asthma phenotype remains rarely understood in Korean children. This study aimed to identify the phenotype of asthma in Korean school-aged children.

Method: We enrolled 674 children with physician-diagnosed asthma from the Korean childhood Asthma Study (KAS) cohort which is a 3-year prospective follow-up study with every 6 months intervals. Physicians verified the relevant histories of asthma and comorbid diseases, as well as airway lability and hyperresponsiveness from the results of pulmonary function and bronchial provocation tests. Questionnaires regarding subjects' baseline characteristics and their environment, self-rating of asthma control, and laboratory tests for allergy and airway inflammation was collected at the time of enrollment. We classified 447 children with asthma from the Korean childhood Asthma Study (KAS) cohort into 4 clusters using hierarchical cluster analysis.

Results: Cluster analysis of the KAS cohort indicated four asthma phenotypes. Cluster 1 (n = 216; 48.3%) of children was characterized by male dominant atopic asthma; cluster 2 (n = 79; 17.7%) was early-onset atopic asthma with atopic dermatitis; subjects in cluster 3 (n = 47; 10.5%) consisted of puberty onset, female dominant atopic asthma having the lowest lung function; and cluster 4 (n = 105; 23.5%) was associated with early onset, less atopic asthma.

Conclusion: Our results indicate that Korean children with asthma can be classified into four distinct clusters. Identification of asthma phenotypes based on our baseline cluster analysis may facilitate prediction of prognosis and response to treatment in heterogeneous phenotype of asthma with follow-up study.

TP1386 | Association between male and female body mass index with lung function parameters in asthma

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Background: Obesity is a significant global public health issue and one of the most common comorbidities in asthma. Patients with increased body mass index (BMI) have greater risk for development of asthma, especially non-allergic phenotype. Increased BMI can be related with asthma severity, as it has been noticed that obese patients with asthma, after weight loss, report decrease in subjective feeling of dyspnea, improvement of spirometric parameters and less frequent disease exacerbations. Our aim was to compare sex related BMI with allergic and non-allergic asthma in order to conclude if sex affects the obesity–asthma relationship.

Method: Case-control study included 149 patients with asthma (group A) and 153 subjects in the control group (group C). Each patient was diagnosed with asthma, with all clinical, functional and inflammatory relevant parameters. BMI was calculated for each patient and control group, as the weight in kilograms divided by the square of the height in meters.

Results: There were more women (61.2%) than man (38.8%) in the group of patients and in the control group (59.4%) as well. The minimal, maximal and median BMI values of group A were 16.9 kg/m^2, 47.1 kg/m^2 and 26.6 kg/m^2 and those values in group C were 18.3 kg/m^2, 36.7 kg/m^2 and 25.1 kg/m^2. Comparison of median BMI values of these two groups shows that examined group of patients had significantly higher BMI (P = 0.004). Population of male showed lower FEV 1 and FEV1/FVC ratio than female, indicating greater airflow obstruction, which is in correlation with their greater BMI (P = 0.044).

Conclusion: These results show that BMI is a significant factor contributing to the development of disease, in association with genetic and other factors. Additionally, in the examined group men showed greater airflow obstruction, possibly because of their greater BMI in comparison with women.

TP1387 | Sensitizer-induced occupational asthma in traditional and industrial bakers

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Background: To assess frequency and characteristics of sensitizer-induced occupational asthma (OA) in traditional and industrial bakers.

Method: We performed a cross-sectional study including 97 bakers (52 males and 45 females, aged 25 to 63 years, duration of exposure at the actual workplace 5 to 29 years), 57 employed in industrial bakery and 39 employed as traditional bakers. Asthma diagnosis was established by standard diagnostic procedure, whereas sensitizer-induced OA was detected by serial peak expiratory flow rate (PEFR) measurements at and away from work and skin prick tests (SPTs) to occupational allergens (wheat, rye and yeast).

Results: Frequency of OA in all study subjects was 8.3%; 7.1% in industrial and 10.2% in traditional bakers (P = 0.604). SPTs to standard and occupational allergens were positive in all subjects with OA. Initial symptoms in all subjects with OA occurred within 4 years after the employment at the actual workplace. In addition, in all subjects with baker's asthma respiratory symptoms were preceded by nasal symptoms (itching, sneezing, rhinorrhea or/and blocked nose).

Conclusion: Our findings indicated similar frequency and characteristics of OA in industrial and traditional bakers confirming bakery as a high risk occupation for OA.

TP1388 | Comorbidities and asthma severity in a Brazilian cohort of patients

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Background: The association between asthma, chronic comorbidities and structural changes in the lungs may explain the more severe and less controlled asthma and should be assessed during the patient approach. Thus, the objective of this study was to verify the prevalence of chronic morbidities, previous occurrence of tuberculosis (TB) and/or pneumonia (PNM) and their association with asthma severity.

Method: This is a cross-sectional study carried out between 2013-2015, when the interest information were collected through questionnaire and clinical evaluation by physician. The data were analyzed through descriptive statistics and compared using Fisher, X^2 and Mann-Whitney U tests. The association was verified through the prevalence ratio and the respective confidence intervals (95% CI) calculation.

Results: A total of 996 patients diagnosed with asthma, classified by severity (GINA, 2012) in two groups were studied: 544 (54.6%) with severe asthma (SA) and 452 (45.4%) with mild/moderate asthma MMA. There was a predominance of females [MMA 350 (77.4%) and SA 446 (82.0%) $P = 0.08$, respectively) in the studied groups and the mean age (years) observed was 36.8 (SD 12.8) in the MMA group and 51.9 (DP13.5) in the SA group ($P < 0.01$). Many chronic morbidities were identified concomitantly to asthma and some were significantly associated to the asthma severity (Table 1). Previous history of PNM and TB was significantly more frequent in SA than in MMA patients. Previous history of PNM [RP 1.68 95% CI (1.48; 1.90)] and TB [RP 1.67 CI 95% (1.47; 1.90)] were associated to severe asthma.

Conclusion: Obesity, rhinitis, osteoporosis, SAH, DM, DLP, hypothyroidism, psychiatric diseases, as well as, previous PNM and TB were significantly more frequent among SA patients. The mean age in this group was also higher, what can explain the more frequent occurrence of comorbidities. In addition, previous history of PNM and TB were associated, respectively, with 1.68 and 1.67 more chances of presenting SA, showing association of past infectious events with asthma severity in this population. Asthma-associated morbidities should be considered in the asthma patient approach and follow-up, since they increase clinical complexity due to disease-disease and disease-drug interactions.

TABLE 1 Frequency of morbidities in patients with mild/moderate asthma and severe asthma

Comorbidities	Mild/Moderate Asthma (MMA) 452 (45.4%)	Severe Asthma (SA) (54.6%)	*P* value
Obesity (IMC > 30)	116 (24.7%)	207 (38.1%)	<0.01
Allergic rhinitis	408 (90.5%)	516 (94.9%)	<0.01
Gastroesophageal reflux disease (GERD)	290 (64.2%)	373 (68.6%)	0.16
Osteoporosis	9 (2.0%)	41 (7.5%)	<0.01
Systemic arterial hypertension (SAH)	77 (17.0%)	243 (44.7%)	<0.01
Diabetes mellitus (DM)	9 (2.0%)	58 (10.7%)	<0.01
Dyslipidemia (DLP)	61 (13.5%)	154 (28.3%)	<0.01
Hypothyroidism	10 (2.2%)	27 (5.0%)	0.03
Hyperthyroidism	0 (0.0%)	5 (0.9%)	0.07
Psychiatric diseases	31 (6.9%)	72 (13.2%)	<0.01
Autoimmune diseases	8 (1.8%)	16 (2.9%)	0.30
Pneumonia (previous)	98 (21.7%)	205 (37.7%)	<0.01
Tuberculosis (previous)	4 (0.9%)	33 (6.1%)	<0.01

TP1389 | Prevalence and clinical characteristics of asthma in children 6-7 and 13-14 years old from Luanda, Angola

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Background: To evaluate the prevalence of asthma and other allergic diseases in children from Angola, and risk factors for asthma, in this population.

Method: This was a cross-sectional study, using the International Study of Asthma and Allergies in Childhood (ISAAC) methodology, in Luanda, Angola between August to November 2014 and March to May 2015, in children from 6-7 and 13-14 years old. Were randomly selected, by municipality, 46 (8%) of 552 primary public schools and 23 (12%) of 186 secondary public schools. Data were analyzed using the SPSS Statistics, v24.0.

Results: The sample consisted of 3080 children of 6 and 7 years old and 3128 of 13 and 14 years old with validated questionnaires. In children of 6 and 7 years old the prevalence of asthma was 15.7%, without significant difference between girls and boys. The assessment of respiratory function by measuring peak flow showed that 49.4%, 47.3% and 3.3% of the children had mild, moderate and severe bronchial obstruction, respectively. The prevalence of rhinitis was 19.0% and of eczema was 18.4%, also without significant differences between girls and boys. In children of 13 and 14 years old, the prevalence of asthma was 13.4%, without significant differences between sexes and the measurement of peak flow in these children showed that 90.3%, 9.5% and 0.2% had mild, moderate and severe bronchial obstruction respectively. The prevalence of rhinitis was 26.9% and of eczema was 20.2%, both were more prevalent in girls. Rhinitis was associated with a greater number of episodes of wheezing and a greater number of episodes of night cough in both age groups with asthma. From the studied risk factors the presence of rhinitis, eczema, a split-type air conditioning system at home, the frequent intake of paracetamol, antibiotics in the first year of life, the frequent truck passage in the street of home, the presence of cats and dogs at home, and passive smoking in particular the mother, were associated with the presence of asthma.

Conclusion: Asthma and related allergic diseases such as rhinitis and eczema, are a public health problem in Luanda. Preventive and control measures should be encouraged.

TP1390 | The association of age of puberty onset and adulthood lung function is mediated by height growth rate in adolescence and its induced DNA methylation in young adulthood

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Background: Age of pubertal events onset is associated with height and lung function in adulthood. It is unknown whether height growth and its associated epigenetics play a role as mediators between ages of pubertal events onset and adulthood lung function.

Method: Data of 434 (227 females) participants in the Isle of Wight (IOW), UK, birth cohort were included in the study. Age of pubertal events onset was obtained by questionnaires at age 18 years. Height at age 10 and 18 years (cm) and lung function parameter (FVC, liter) at 18 and 26 years of age were measured. Genome-scale DNA methylation (DNAm) at age 18 years was analyzed using Illumina Infinium arrays (450K and EPIC). Path analyses using structural equation models were used to examine the association of age of pubertal events onset and lung function at adulthood, and the mediating effects of height growth during adolescence and DNAm at age 18 years. Height growth associated CpGs were identified using the *ttScreening* R package. The findings were tested in the independent ALSPAC cohort.

Results: In the IOW, DNAm at 35 CpGs showed an association with height growth as well as pubertal events. Through path analyses, age of menarche of females had positive indirect effects on FVC at age 26 years (coefficient = 0.21; $P < 0.0001$) via height growth. The effects of age of menarche were further mediated by DNAm at age 18 at cg08680129 (age of menarcheàDNAm (age 18 years) àFVC (age 26 years), coefficient = 0.044, $P = 0.03$; age of menarche àheight growth àDNAm (age 18 years) àFVC (age 26 years), coefficient = 0.23, $P < 0.0001$). For males, age of growth spurt (coefficient = 0.12; $P = 0.003$) had positive indirect effects on FVC at age 26 years via height growth. Indirect effects of ages of menarche on FVC at age 24 years via height growth in ALSPAC were consistent with those at 26 years in IOW.

Conclusion: Height growth in adolescence and DNAm at age 18 mediate the association of age of pubertal events onset with adulthood lung functions.

TP1391 | Prevalence and risk factors in bronchial asthma in children of 6-7 years old and adolescents of 13-14 years old in the municipality of Puerto Vallarta, Mexico

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Background: Bronchial Asthma is the most frequent chronic airway disease worldwide. Characterized by recurrent episodes of dyspnea, wheezing, chest tightness and cough, with variations of severity and frequency. There are risk factors to develop such as atopy, exposure to allergens, and particles like dust mites, pollution, pet dander, pollens and molds, tobacco smoke, viral infections, diet, gender, physical activity and medications. The weather of Puerto Vallarta is semitropical and humid. *Objective*: Determine the prevalence and risk factors in bronchial asthma, in children of 6-7 and adolescents of 13-14 years old in Puerto Vallarta, Mexico.

Method: Cross-sectional study, based on the ISAAC questionary, applied to children from 6-7 and adolescents from 13-14 years old. Statistical analysis SPSS 20.0 applying Chi-square test, calculating the odds ratio (OR) and 95% confidence interval, considering statistical significance ($P \leq 0.05$).

Results: 2244 children of 6-7 were included: 45.6% male, 54.4% female and 2479 teenagers of 13-14 46.1% male, 58.9% female. The prevalence of asthma in the group of 6-7 was 9.2% and 13-14 was 9.5%. Regarding risk factors, atopy was the factor present in both groups. In schoolchildren the consumption of paracetamol either during the pregnancy, in the last 12 months or the first year of life for the presence of cough or wheezing, as well as contact with cats in the last 12 months and dogs in the first year of life, maternal smoking during pregnancy, premature child, bronchial infections and ingestion of antibiotics; As a measure of sedentary lifestyle, children who spent 1-3 hours in front of a screen had more association with the presence of wheezing in children. In adolescents, an association was found between active smoking at 9 years of age and the intake of paracetamol in the last 12 months with the presence of wheezing ($P \leq 0.05$).

Conclusion: We found a higher prevalence of asthma than reported in this area and risk factors similar to other studies. We found a higher prevalence of asthma than reported in this area and risk factors similar to other studies

TP1392 | Lung function decline in elderly asthma: 3-year follow up in prospective study

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Background: Asthma in the elderly (age ≥ 65 year-old) is increasing and poses a great socioeconomic burden on the health care system. We investigated annual lung function decline among in elderly asthma cohort during 36 months.

Method: Three existing adult asthma cohorts in Korea merged into elderly asthma cohort with a unified protocol and database. We selected a total of 1382 patients from the merged cohort to evaluate risk factors predicting acute exacerbation during one year prior to the enrollment. Baseline data were collected on clinical variables, smoking history and atopic status. Exacerbation and longitudinal lung function change was observed over a period of 3 years. Lung function decline was compared using a linear mixed effect model for longitudinal data.

Results: Overall, the elderly asthma patients experienced a rate of decline of lung function (Forced expiratory volume in 1 second, FEV1) of 49 ± 5.8 mL per year. Among subjects who participated in 36 months, the adjusted decline in FEV1 among subjects with exacerbation in asthma was −64 ± 5.32 mL per year, as compared with −46 ± 5.71 mL per year in those without exacerbation (P = 0.036). Independent factors associated with an accelerated decline of lung function were more frequent severe exacerbations, baseline fixed airway obstruction and chronic sinusitis.

Conclusion: In our prospective study, recurrent exacerbation and fixed airway obstruction are associated with lung function decline in elderly asthma.

TP1393 | Asthma hospitalizations – what changed in the last decade?

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Background: Prevention of exacerbations is one of the main goals in the treatment of respiratory diseases worldwide. Despite of prevention measures implementation, moderate/severe exacerbations still occurs and need hospitalization. The aim of this study was to analyze the asthma disease characteristics of hospitalized patients in an allergology department, during 2017, comparing it with hospitalized patients in 2006.

Method: Retrospective study. We analyzed the demographic data, the disease characteristics before the hospital admission (treatment, follow-up, previous hospitalizations) and the characterization of the exacerbation (severity, triggers and the duration of the hospitalizations).

Results: Asthma exacerbations led to 29 hospitalizations in 2006 and 41 in 2017. In the table below, we present the analyzed data. No deaths were recorded. Only 1 patient was re-admitted in 2017.

Conclusion: Comparing both periods, we verified that in 2017 there was a reduction in the number of patients without prior follow up, and also, a reduction in the number of patients without an asthma action plan. This data suggests a favorable evolution of secondary prevention, despite the small population. However, we found

	2006	2017	*P*-value
N	29	41	
Female gender (%)	58.6	70.7	0.293
Age (average ± std deviation, years)	42.9 ± 16.7	49.8 ± 21.5	0.138
Previous asthma hospitalizations (%)	10.3	70.7	<0.001
Previous follow up (%)	75.9	92.7	
Previous treatment (%): SABA Inhaled corticosteroid alone LABA alone LABA + Inhaled corticosteroid ARLT	79.3 58.6 13.8 13.8 20.7 6.9	90.2 41.5 4.9 0 80.5 63.4	0.157 <0.001 <0.001
Exacerbation severity: moderate, severe (%)	63; 37	71.1; 28.9	0.492
Exacerbations triggers (%): Respiratory infection Allergen exposure Combustion agent's exposure Poor therapeutic adherence Unknown cause	79.3 10.3 6.9 3.4	43.9 2.4 2.4 22 29.3	0.003 0.006
Duration of hospitalization (average ± std deviation, days)	9 ± 3.1	11.1 ± 5.9	0.077

an increase in number and duration of hospitalizations, with a high number of patients with previous asthma hospitalizations, as well a high number of asthma exacerbation due to poor therapeutic adherence. This data supports and enhance the need of reinforce the importance of therapeutic adherence.

TP1394 | Causes behind admission to pediatric intensive care unit (PICU) in asthmatic patients in Qatar

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Background: Most Pediatric asthma exacerbations are managed in emergency centers while more severe cases that fail to respond to treatments require admission to Pediatrics Intensive Care Units (PICU). This retrospective study investigates the reason behind severe Asthma attacks that require PICU admission in children in Qatar, through the years 2001-2017.

Method: Data about Asthmatic patients who aged between 6-14 years admitted to PICU was collected from medical records of Hamad Medical Corporation.

Results: Severe Asthma exacerbation was the reason of admission in 52 out of 2627 files reviewed for PICU admissions in the same age range. Males represented 57%, mean age was 9.13 years, no deaths were recorded. Upper Respiratory Tract Infections (URTI) were seen in 41(69%), and URTI combined with other environmental triggers (exercise, dust, paint fumes and animal dander) seen in 8 (13.5%). Exercise induced bronchospasm was seen in 4, and unknown reasons in 3. Other triggers with one admission each were tobacco smoke, dusty weather, and emotional stress. Viral studies were done in 12; Rhinovirus was detected in 6, Adenovirus in 2, and 1 for each Corona and Enteroviruses. Mycoplasma antibodies were positive in 10, MRSA in 4, and 1 for each Streptococcus Pneumoniae, Haemophilus Influenza, and gram-positive coccobacilli in either blood or sputum cultures.

The PICU admission was the first Asthma presentation in 6, while repeated attacks were in 7, all were atopic, 6 allergic rhinitis, 2 food allergy, 2 drug allergies, with Tobacco exposure in 2. Specialist follow up was in 4 patients, 2 after 1st admission, and never in 3. The only one compliant with control medication was from the third group.

Among the 39 single admissions, 12 were following with specialists; adherence to medication was seen in 6, unknown for 2. Remaining 27, either stopped following with specialized clinics, followed with non-specialized clinics or private health care, 12 had controller medication, compliance seen in 1.

Conclusion: A shortage of awareness, poor adherence to medication, and need for specialist evaluation by the patients and families was the main reason behind PICU admissions among Asthma patients in Qatar. Indicating the importance of increasing disease understanding in general populations.

TP1395 | Inhaled corticosteroids are associated with increased pneumonia risk in asthma patients

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Background: Asthma is a common disease that is an expensive burden to patients. Inhaled corticosteroids (ICS) are the most important drugs for asthma treatment and should be maintained to control asthma. However, the use of ICS has been reported to increase pneumonia and this is still controversial. We evaluated whether the use of ICS increases the risk of pneumonia in asthmatics using the Health Insurance Review and Assessment Service (HIRA) database in Korea.

Method: The Asthma Management Adequacy Assessment was performed by the HIRA in Korea. Patients who were prescribed asthma medications more than 2 times with claimed insurance benefits of asthma disease codes were enrolled. Demographics of patients, asthma medications, healthcare use, and complications were analyzed.

Results: The number of asthma patients was 831 613. Age of patients using ICS and those without ICS were 57.9 and 56.7 years and ICS users had higher Charlson comorbidity index than patients not using ICS. The most common comorbidities were allergic rhinitis and hypertension. The proportion of patients using ICS was higher in tertiary hospital type. They visited outpatient clinics, emergency rooms, and were hospitalized more often, even to intensive care unit. They also had more pneumonia, empyema, acute respiratory failure, pneumothorax and pneumomediastinum. In addition, they used more respiratory medications, such as long/short-acting β–agonists, long-acting muscarinic antagonists, leukotriene receptor antagonist, except theophylline. Multiple logistic regression analysis showed that ICS prescription was associated with pneumonia (OR 1.38; 95% CI 1.36-1.41). Age, sex, medical care, use of secondary and tertiary hospitals, and hospitalization due to asthma in the previous year were associated with pneumonia in addition to ICS prescription.

Conclusion: ICS use was associated with increasing pneumonia in asthma patients in Korea. Therefore, it is critical to acknowledge that the use of ICS in asthmatics may increase the risk of pneumonia and follow up with preventative efforts.

TP1396 | Age and obesity are associated with increased asthma severity in algerian patients with allergic asthma

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Background: Asthma is a heterogeneous disease defined as a chronic inflammatory disorder of the airways. The most common type of asthma is allergic asthma. The prevalence of asthma in the Maghreb countries is moderate, but its impact on patient's life is high. In Algeria, Asthma incidence rates was 46/10 000 in 2009. However, this rate is underestimated given the lack of epidemiological study in Algeria. Our aim in this study was to assess whether age and obesity are related or not with asthma severity in Algerian patients with allergic asthma.

Method: The evaluation of the asthma type was carried out by a specialist according to the GINA classification. The clinical data were obtained in the presence of the patients (N = 135) and their doctor between 2016 and 2018 in the locality of Rouiba, east of Algiers. A free and informed consent has been signed by patients.

Results: Clinical data showed that the sex ratio of our cohort M/F (45/90) was 0.5, suggesting that there are 2 times more women with asthma than men. Patients with mild (N = 23), moderate (N = 63), and severe asthma (N = 49) had an average age of 40, 50, and 55 years, respectively. Interestingly, we have found that severe asthma is associated with obesity. In fact, 70.6% of patients with severe persistent asthma, 54.2% of patients with moderate persistent asthma, and 47% of patients with mild persistent asthma have a body mass index (BMI) > 25.

Conclusion: Our study suggests that in the Algerian population, women are more often affected with asthma than men. Moreover, the severity of asthma increases with age and obesity.

TP1397 | Factors related to treatment response in cough variant asthma

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Background: The diagnosis of cough variant asthma (CVA) is mainly based on the presence of chronic cough, normal spirometry, bronchial hyperresponsiveness (BHR) and a favorable response to anti-asthmatic therapy. However, the response rate is variable. The aim of the study was to assess the response to treatment and factors related to treatment efficacy in patients with suspicion of CVA.

Method: The study included 33 patients with chronic cough, no signs of wheezing or dyspnea, in whom spirometry, chest X-ray were normal and BHR was confirmed (PC_{20}<16 mg/mL). The anti-asthmatic treatment was applied in 3 consecutive steps:

1. inhaled corticosteroids in medium dose and long acting beta-agonist; in patients with no improvement after 4-6 weeks the 2nd step was added
2. leukotriene receptor antagonist; in the absence of improvement after 4-6 weeks the 3rd step was added
3. oral prednisone (30 mg/d) for 10 days.

Favorable response to treatment was defined as an increase in quality of life (QoL) in Leicester Cough Questionnaire (LCQ) > 1.3 point and as a reduction of cough severity > 20 mm in visual analogue scale (VAS). In patients who responded to any of these steps, CVA was diagnosed.

Following factors were included in the analysis of treatment efficacy: cough duration, QoL in LCQ, cough severity in VAS, PC_{20}, FeNO, differential cell count in induced sputum (IS), blood eosinophil (EOS) number and percentage and severity of BHR (<1, 1-4, >4 mg/mL).

Results: As 29 patients responded to anti-asthmatic therapy, CVA have been diagnosed in 29/33 (88%) of them. 64%, 18% and 6% of patients reported the improvement after the 1st, 2nd and the 3rd step of therapy, respectively. The median reduction of cough severity in patients with CVA was 27 mm (IQR 20-49) in VAS and the median increase in the QoL in LCQ was 4.9 points (3.5-6.5).

There was no correlation between cough severity and PC_{20}, FeNO, blood or IS EOS. Decrease in cough severity as a result of treatment correlated with initial blood EOS percentage and FeNO (r = 0.55, P = 0.002 and r = 0.59, P = 0.001, respectively) but not with PC_{20} or IS EOS.

Conclusion: The majority of patients with clinical features of CVA respond well to anti-asthmatic treatment. Neither cough severity nor decrease in cough severity as a result of treatment depends on PC_{20}. Blood EOS and FeNO may be predictors of response to anti-asthmatic therapy in CVA.

TP1399 | Exacerbations in patients with severe asthma

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Background: Severe asthma represents 5-10% of all asthmatic patients. In the last decades, specific Severe Asthma Units have been developed to meet the needs of this high resource demanding subset of patients. Despite this close follow-up, exacerbations and, therefore, their causes are a fundamental problem that needs addressing. The objective of this study was to find potential predicting factors of these exacerbations.

Method: To evaluate the causes of exacerbations in this subset of asthmatic patients, a retrospective study was developed. We analyzed all patients (n = 123) that visited our Severe Asthma Unit in 2017. Inclusion criteria comprehend: patients diagnosed with severe asthma, with at least 3 months of follow-up and age > 16 years. Analyzed variables

included: age, sex, comorbidities (atopic dermatitis, intrinsic/extrinsic asthma, rhinoconjunctivitis, nasal polyposis, gastroesophageal reflux disease and obesity), asthma treatment, number of visits to the Severe Asthma Unit and worst spirometry results in 2017. In the exacerbations group, time passed since last visit to the Severe Asthma Unit and since last spirometry were also recorded.

Results: 123 clinical records were analyzed, of which 26 patients were excluded for not meeting the inclusion criteria. Of the resulting 97 patients, 21 (22%) presented exacerbations. Most frequent comorbidities found were rhinoconjunctivitis (69%) and gastroesophageal reflux (30%). Aside standard treatment, 22 (22%) patients received Omalizumab and 2 (2%) Mepolizumab. Mean visits in the non-exacerbations group were 3 and 4 in the exacerbation group. Mean spirometry FEV1/FVC and FEV1 were, 69 and 88% in the non-exacerbation group, and 66 and 86% in the exacerbation group, respectively. A statistically significant association was found between the presence of obesity ($P < 0.01$) and exacerbations, but was not found for the other variables studied.

Conclusion: Despite the close surveillance severe asthma patients have, there is still a 22% of them who present exacerbations, partly explained by the presence of comorbidities, such as obesity. More studies in this line are needed as to ascertain the degree of impact other comorbidities, number of visits and spirometry results have on the control of these patients.

TP1400 | Correlation of serum vitamin D level and asthma control: A cross-sectional study from Jeddah, Saudi Arabia

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Background: Some studies suggest a possible role of vitamin D in asthma control. The aim of this study was to investigate the potential relationship between low serum vitamin D with asthma control.

Method: A cross-sectional study of consecutive patients with the diagnosis of asthma from the outpatient clinic at King Abdulaziz University hospital was analyzed between January and December 2011. They were classified according to their asthma control level. Measurement of serum vitamin D was performed. SPSS was used to examine any statistical correlation.

Results: Sixty-four asthmatic patients were included in this study; 31.25% (n = 20) males and 68.75% (n = 44) were females. Serum 25-hydroxyvitamin D deficiency (Less than 50 nmol per litre) was found in 84.3% (n = 54), insufficiency (50 to 74.9 nmol per litre) in 14.1% (n = 9), and sufficient serum level (75 nmol per litre or greater) in 1.6% (n = 1) patients. Level of asthma control assessment revealed 25 (39%) uncontrolled, 27 (42.2%) partially controlled and 12 (18.8%) controlled patients. Low vitamin D was found in 12 (19%) controlled versus 51 (81%) in non-controlled asthmatics. There was no significant statistical correlation found between low serum vitamin D level and asthma control (P value 0.85).

Conclusion: Low vitamin D was prevalent in more than three-quarters of patients with asthma. The relationship between low serum vitamin D level and poor asthma control showed a trend but was not statistically significant. Further studies are needed to explore the association of low vitamin D with asthma control.

TP1401 | Longitudinal study of risk factors for asthma exacerbations in Chinese schoolchildren

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Background: Asthma exacerbation is an important cause of impaired lung function in children. Cross-sectional studies implicated human rhinovirus (HRV) as a major risk factor for asthma-associated hospitalizations. However, there is limited evidence from prospective studies to confirm such relationship. This study investigated the associations between asthma exacerbations and HRV infection and environmental factors in Hong Kong children.

Method: Chinese children aged 6-17 years with history of asthma exacerbations within previous 12 months were recruited. Skin prick tests with locally prevalent aeroallergens and Chinese ISAAC questionnaire were used to evaluate atopy and early-life and environmental exposures respectively. During September-December, home visits were arranged every 2-4 weeks to follow patients for their asthma control using both symptom diary and Asthma Control Test. Patients also underwent spirometry and fractional exhaled nitric oxide (FeNO) measurement at each visit. Flocked nasopharyngeal swabs (FNPS) were collected for HRV detection by molecular assay. Kaplan-Meier analysis was used to analyze the effects of patient and environmental factors as well as presence of HRV infections on asthma exacerbations.

Results: The mean age (SD) of 33 asthmatic patients (17 males and 16 females) was 10.8 (3.0) years, and 85% of them were allergic to house dust mites. Six cases dropped out during follow-up. Ten (37%) subjects developed mild-to-moderate asthma exacerbations but none required hospitalization. The remaining 17 subjects were grouped as "stable asthma". Totally 164 FNPS samples were collected, among which 41 (25%) were positive for HRV. Baseline spirometric indices and FeNO were comparable between children with asthma exacerbations and stable asthma. None of the assessed factors was significantly associated with asthma exacerbations, although there was a trend towards more events among children exposed to domestic tobacco smoke. Paradoxically, children free from any HRV infection might have a higher rate of disease exacerbations during surveillance. Other patient or environmental factors were not associated with childhood asthma exacerbations.

Conclusion: Domestic tobacco smoke exposure is a possible risk factor for disease exacerbations in Chinese school-age children with asthma, whereas this prospective study cannot confirm any relationship between HRV infections and childhood asthma exacerbations. (funded by Hong Kong Institute of Allergy Research Grant 2017)

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DRUG HYPERSENSITIVITY: EPIDEMIOLOGY, MECHANISMS AND DIAGNOSTICS

TP1402 | Severe cutaneous adverse reactions to drugs in latin America: An update of racgrad study

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Background: Severe cutaneous delayed drug reactions (SCARS), including Toxic Epidermal Necrolysis (TEN), Stevens-Johnson Syndrome (SJS), Acute Generalized Exanthematous Pustulosis (AGEP) and Drug Reaction with Eosinophilia and Systemic Symptoms/ Drug-induced Hypersensitivity Syndrome -DRESS/DiHS-), are rare but potentially fatal complications of drug treatment. Although its epidemiology has been described in different countries, it is unknown in Latin America. Our aim was to describe the epidemiological characteristics of severe cutaneous reactions to drugs in five countries in Latin America.

Method: This is a cross-sectional, descriptive, multicenter, Latin American study of patients diagnosed with SCARs, between January 2009 and December 2018. We used a modified and adapted version of ENDA questionnaire for drug allergy interesting group. Demographic data, type of reaction, culprit drug(s), treatment, complications, mortality and sequelae, were included. Five countries (Colombia, Argentina, Brazil, Paraguay and Peru) participated. The analysis was made from a database in BDClínic.

Results: Seventy two cases were reported. Two were excluded because they were duplicated. Seventy patients were available for analysis. Forty two (61%) were women. The median age was 38 years. Forty two (61%) had DRESS/DiHS, 12 (17%) TEN, 5 (7%) SJS, 6 (8.5%) AGEP, 4 (6%) other not classified SCARs, and 1 (1%) overlapping TEN/SJS. The main culprit drugs were aromatic anticonvulsants in 31 cases (44%), beta lactam antibiotics in 9 (13%) and non-beta lactam antibiotics in 8 (11%). In all patients the suspect drug was withdrawn. Sixty six patients (94%) received systemic anti-inflammatory treatment (mostly corticosteroids). Complications occurred in 40 cases (57%) and death in three patients (4%). Thirteen patients (18.5%) had some type of sequel.

Conclusion: This is the first study that describes demographic data, epidemiologic and clinical characteristics of SCARs in several centers of five Latin American countries. DRESS/DiHS was the most frequently reported clinical entity and anticonvulsants were the main triggers. Most of patients received systemic anti-inflammatory treatment. Complications were frequent, but mortality was low.

TP1403 | Development and validation of questionnaire for study of drug allergy among armenian population

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Background: In Armenia as worldwide drug allergy (DA) is considered a serious healthcare problem. The urgency of problem depends on the increase of drug use, the lack of unified principles of diagnostics, treatment and prevention, the presence of life-threatening manifestations. One of the aims of our survey is to study the DA prevalence among population.

Method: Our work is performing in the frame of grant project № 18T-3B157 of State Committee of Science of RA. It is approved by Committee of Bioethics of YSMU. According to the main principles the original questionnaire for study of DA among Armenian population was developed by us. For validation of the questionnaire the pilot study was performed among university students. In introduction it was stated that the study is voluntary and obtained data would be used for research only. The questionnaire was completed by the questions on adverse reactions to drugs, their manifestations; causative drugs and risk factors; hospitalizations, treatment and diagnostic measurements; co-morbid allergic and non-allergic diseases, etc.

Results: 437 of filled preliminary questionnaires (response rate - 97.1%) were appropriate to analysis. 39 (8.9%) of students (14 males & 25 females) with mean age 20.8 ± 1.2 reported about lifetime adverse reactions to drugs. The following manifestations were mentioned: skin rushes (urticaria, eczema, edema, etc.) – 37 (94.9%), anaphylactic shock – 2 (5.1%), respiratory – 12 (30.8%), other – 5 (12.8%). The following drugs were mentioned as causative: non-steroidal anti-inflammatory – 14 (35.9%), antibiotics – 8 (20.5%), other (local anesthetics, vaccines, etc.) – 6 (15.4%), unknown – 11 (28.2%). 22 (56.4%) of students have ever visited a doctor/been hospitalized for reactions to drugs, 12 (30.8%) – have verified diagnosis of co-morbid allergic disease (asthma, allergic rhinitis, atopic dermatitis, etc), 5 (12.8%) – have food allergy. From non-allergic diseases mainly the chronic ENT diseases and frequent colds were mentioned by 16 (41.0%) and 12 (30.8%) of students, respectively.

Conclusion: In the process of validation of questionnaire some inconsistencies were found in the respondents' answers, which in our opinion was due to the unclear wording of question. Thus, one question was added and some variants of answers were clarified so that the final questionnaire included both the parts of demographic data and questions on DA. It can be concluded that after all corrections the original questionnaire is ready to implementation.

TP1404 | Adverse drug events and drug hypersensitivity reactions leading to emergency department visits: An observational study in four university hospitals

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Background: Adverse drug events (ADE) and drug hypersensitivity reactions (DHR) have been recognized as an important cause of serious morbidity and mortality. Severe cases of ADE requires immediate medical treatment including Emergency Department (ED) visits. We estimated the prevalence and features of ADE leading to ED visits.

Method: We established study consortium of 4 tertiary university hospitals in Korea. Applying a standardized study protocol and web-based reviewing system, we retrospectively reviewed electronic medical records and the National Emergency Department Information System data of all patients who visited ED from January 2016 to June 2016. Trained nurses firstly screened the potential ADE cases, and then allergy specialists or pharmacist confirmed ADE cases and specified the causative drugs, phenotype, causality and final diagnosis in each ADE.

Results: ADE-related ER visits were more common in female and elderly. The side effect was the most common type of ADEs, followed by DHR and overdose. Preventable ADEs comprised about one of six cases. The common causative drugs were antineoplastic drugs, antithrombotic agents, drugs used in diabetes, antibacterial drugs, and anti-inflammatory and anti-rheumatic drugs based on the Anatomical Therapeutic Chemical Classification System.

Conclusion: The prevalence of ADE leading to ED visits was high in this study. Cases were significantly more frequent in older adults and females. Many cases of ADEs were preventable and predictable. DHR was one of the frequent causes of ADE leading to ED visits.

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TP1405 | Knowledge and attitudes regarding drug allergy among residents and interns in Tracia region of Turkey; a multicenter study

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Background: Drug allergy (DA) is one of the most important reason of iatrogenic morbidity and mortality. Proper management of DAs is imperative and crucial for the patients. Currently DA remains a little known issue for health care professionals; regardless of their educational status or level of hospital they are working.

Method: A cross-sectional survey was conducted in 3 university hospital of Tracia region of Turkey. The study population included 6th grade medical students (interns) and residents from all clinical specialities. The study was approved by Trakya University's ethical committee. Participants were asked to fill a questionnaire in which their knowledge level and attitudes against DA were assessed.

Results: The final number of respondents who completed the survey was 630. Demographic characteristics of participants were summarized in Table-1. Residents had higher knowledge score (3.9 ± 1.1) compared with interns (3 ± 1.2) ($P < 0.001$). The average year in practice of residents was 2.5 ± 1.5 year and 81% of them were under 3 year. The knowledge scores of residents were correlated with experience time ($P < 0.05$). The answers about knowledge and attitudes related DA were summarized in Table-2 and Table-3.

Conclusion: We assessed the knowledge and attitudes regarding (DA)s among residents and intern doctors in Tracia region of Turkey and found low level of knowledge and awareness. Future studies involving a larger sample size may lead to revision in curriculum of pre and postgraduate medical education regarding (DA)s.

Age (year) Median (Min-Max)	26.1 (21-38)
Gender n (%)	Female 347 (56) Male 274 (44)
Education status n (%)	intern 292(46) Resident 338 (54)
Year in practice (residents) n (%)	<3 year 262 (81) >3 year 61 (19)
Specialty group (residents) n (%)	Internal 210 (62) Surgery 129 (38)
Education about DA as a separate lecture during medical education n (%)	Yes 208 (33) No 421 (66.8)
Weekly frequency of encountering with the patient who states (he/she) has drug allergy n (%)	<%5: 337 (54.7) %5-25: 202 (32.8) >%25: 74 (12.5)
Participation or observation to any drug provocation test before n (%)	Yes 32 (5.1) No 593 (94.99

Question/Choices	True answers
«Which one should be first choice in the treatment of drug related anaphylaxis ?» A) Systemic antihistaminics B) Systemic glucocorticoids C) *Epinephrine* D) Dopamine	533 (84.7)
«Which one is the most common clinical sign of drug allergy?» A) Elevated transaminases B) *Skin rush* C) Serum disease D) Anaphylaxis	535 (85.1)
«A desensitization procedure can be used for patient treatment in which of the following drug reaction?» (check all that apply) A) Phenytoin induced toxic epidermal necrolysis B) Cotrimoxazole induced Stevens-Johnson syndrome C) *Meropenem induced anaphylaxis* D) *Shortness of breath, wheezing and nasal obstruction due to the use of aspirin in the patient with asthma and nasal polyps*	361 (63.1)
«If an anaphylactic reaction to a drug is suspected, which of the following tests may be ordered for confirmation of anaphylaxis?» A) Plasma histamine B) Serum specific IgE level C) *Serum total tryptase* D) C1q binding assay E) I don't know	90 (14.5)
«What percentage of patients with a history of penicillin allergy can tolerate penicillin?» *A) > %75* B) %51-75 C) %26-50 D) %16-25 E) %0-15	74 (11.8)
«Skin tests can be used for evaluation in which of the following drug reaction?» Check all that apply A) Digoxin induced cardiac arrhythmia B) Vaginal candidiasis due to ciprofloxacin C) *Morbilliform rash due to amoxicillin clavulanate* D) Electrolyte imbalance due to furosemide	465 (75.6)

Question	Choices	Answers
«Education of doctors about drug allergy is absolutely essential»	I agree	581 (92.2)
	I don't agree	12 (1.9)
	I am not sure	35 (5.6)
«I definitely know what should I do in the case of a patient who has clinical signs of drug allergy»	I agree	178 (28.3)
	I don't agree	108 (17.1)
	I am not sure	344 (54.6)
«It is necessary to determine drug allergy by in-vitro or in-vivo tests, before administering any medication to any patient»	I agree	241 (38.3)
	I don't agree	233 (37)
	I am not sure	154 (24.5)
«I take drug allergy history when prescribing any medication»	No, I have no time	22 (3.5)
	Sometimes	89 (14.2)
	Usually	253 (40.3)
	Always	264 (42)
«If one of your patients reports a drug allergy and you do not believe that the patient is truly allergic to that medication, do you still give the medication?»	Yes	67 (10.7)
	No	407 (64.9)
	Sometimes	153 (24.4)

TP1406 | The last 12 years of a contrast media allergy consultation

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Background: Contrast Media (CM) are used in a wide variety of diagnostic and therapeutic procedures. Although CM are safe products there have been described some allergic reactions. The objective of the study was to characterize the patients (pts) with a suggestive history of hypersensitivity to CM.

Method: Retrospective observational study in which the patients observed in a CM Allergy consultation between June 2006 and June 2018 were selected. Patients were characterized as to demographic data, personal history, presence of atopy, drug hypersensitivity, prophylaxis, route of CM administration, time between CM administration and the reaction and type of CM.

Results: A total of 236 pts were selected, 64% (152 pts) of which were female, with an average of 53.29 years in the first allergic reaction and 58.03 years in the first consultation, with an average between the first reaction and the first consultation of 4.74 years. The most common route of administration was intravenous (63% - 153 pts). The examinations that were more frequently involved in reactions were CT scan (42% - 99 pts) and coronarography (19.1% - 45 pts). The most frequent personal history was heart disease (36.3% - 114 pts), rhinitis (29% - 91 pts), renal insufficiency (15.3% - 36 pts)

and asthma (10.6% - 25 pts). From the 236 pts, 20.3% (48 pts) had a history of atopy and 20.3% (48 pts) had a history of drug hypersensitivity. From the patients with risk factors (79.2% - 187pts), only 6.4% (12 pts) performed prophylaxis with antihistaminic drugs and/or corticosteroid. Fifty percent of the reactions happened within 1 hour after CM administration and 48% were late reactions; the remaining 2% were unaware of the time interval between CM administration and the beginning of the reaction. Seventy-eight percent (184 pts) identified as the cause of the reaction an iodinated CM, 8.4% (20 pts) a non-iodinated CM and 13.6% (32 pts) did not know which CM was involved. The most frequently identified CM was iodinated iodixanol: 19% (44 pts).

Conclusion: The most frequently identified CM was iodixanol, which can be due to the fact that CT scans were the most frequently examinations involved and also because this is the most CM widely used. It can be also concluded that most of the personal history described are risk factors for reaction to CM and that most patients with risk factors did not perform prophylaxis prior to CM administration, which may justify a higher probability of reaction.

TP1407 | True penicillin allergy in internal medicine hospitalized patients

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Background: Penicillin allergy is the most common reported drug allergy on hospital admissions. This diagnosis is often inaccurate and associated with a clinical and economic burden since it implies treatment with a less effective and costly second line therapy. This drug allergy is the easiest to confirm and the cost associated with the study is significantly lower than the one associated with the false diagnosis. The aim of our study was to determine the prevalence of the true allergy to penicillin in patients hospitalized in the Internal Medicine department of a district hospital, as well as the rate of registration in the Drug Adverse Reaction Portuguese Catalog (CPARA).

Method: A prospective study was performed enrolling patients hospitalized in the Internal Medicine department between February and June 2017. The patients labeled as allergic to penicillin were interviewed concerning their allergy history and data related to the hospitalization was collected. They were referred to the allergology department and submitted to the allergy workup for diagnostic confirmation according to the EAACI Guidelines.

Results: From the 680 hospitalized patients, 40 (6.2%) claimed to be allergic to penicillin, being 70% female (n = 28), mean age of 75.6 ± 11.4 years. Considering the patients with antibiotherapy indication, 16 were treated for a respiratory infection, 4 for urinary tract infection and 1 for colitis. The most used alternative antibiotic was ceftriaxone mostly combined with azithromycin. The clinical condition of 10 patients didn't allow the interview and further investigation and 14 missed the follow-up appointment. The reaction had occurred less than 10 years before in 5 patients, 10 to 20 years before in 5 and more than 30 years in 26. The clinical manifestations reported were: angioedema in 5, exanthema in 8, urticaria in 3, other reactions in 5 and 13 patients couldn't remember.

The workup confirmed the allergy in 1 patient and in other allergy had been diagnosed in a previous study. Three patients had negative study results and 1 abandoned the study. Ten patients were verified on clinical records having been treated with aminopenicillin and were not studied. The 2 allergic patients and 11 of the remaining had been registered on CPARA.

Conclusion: Penicillin allergy is overreported by patients hospitalized in Internal Medicine department. Whenever possible clinical files should be sought for previous prescriptions or allergy workup should be carried out. CPARA data are frequently not confirmed.

TP1408 | Drug hypersensitivity reactions to cephalosporins

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Background: In the past decades, cephalosporin hypersensitivity has been mostly studied in the context of penicillin allergy, as an alternative drug. Nowadays cephalosporins are widely used both for common infections and as first-line prophylaxis for surgical procedures becoming more commonly associated with allergic reactions. Our aim was to describe the patients with an allergy workup for cephalosporin allergy in our experience.

Method: We included 478 patients who reported an HDR to cephalosporin and underwent an allergology workup between January 1992 and July 2018 in the Allergy Unit of the University Hospital of Montpellier (France). Logistic regression analysis was used to search for risk factors for hypersensitivity to cephalosporin (positive skin test or provocation test results).

Results: In the studied population, 65% of patients were female and 31% were < 18 years old at the time of the reaction. Atopy was present in 40% of the patients, 15% were asthmatics. The most common clinical manifestation involved the skin (urticaria and/or angioedema in 36% and maculopapular exanthema in 21%) followed by anaphylaxis in 34% of the patients (half of them with shock). One-third of the reactions were immediate (<1 hour), 56% were delayed (>1 hour) and 26% of the patients reported multiple episodes. DHR was confirmed in 111 patients (23.1%), 58 through skin tests and 53 through DPT. From those, 46.5% reported an immediate reaction and 12% a non-immediate reaction. The risk factors identified for having a DHR

to cephalosporins were: having a clinical history of an immediate reaction (OR:3.2, CI 1.8-5.7); clinical history of anaphylaxis (OR:2.8, CI 1.5-5.5); clinical history of anaphylactic shock (OR: 5.2, CI 2.7-10) and history of multiple episodes (OR:1.8, CI 1-3.1).

Conclusion: Near ¼ of the patients had confirmed DHR to cephalosporin. The patients with a higher probability of having a DHR to cephalosporins were those with a clinical history of immediate reaction, anaphylaxis (higher risk in anaphylactic shock) and history of multiple episodes.

TP1409 | Biotin labeled clavulanic acid to deepen analysis of serum proteins target of haptenation: Implication in betalactams allergy studies

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Background: Clavulanic acid (CLV) is a betalactamase inhibitor frequently administered combined with amoxicillin (AX). Both betalactams (BLs) can be independently involved in allergic reactions. Indeed, selective immediate allergic reactions to CLV have recently been reported in 30% of patients allergic to AX-CLV. Although protein haptenation with BLs is considered necessary to activate the immune system, currently there are no straight-forward detection tools, such as a monoclonal antibody against CLV, for the study of protein haptenation with CLV. Preliminary CLV haptenation studies have suggested similar target proteins of AX, although in depth studies are still necessary to identify specific candidate proteins of CLV. The objective was to study haptenation by CLV and identify its target proteins.

Method: The experimental design included the labeling of CLV with biotin, then incubation with either human serum albumin (HSA) or sera and, finally, the resulting protein adducts were analyzed by different techniques. Biotinylated CLV (CLV-B) was synthesized by introducing a biotin moiety in the carboxylic group of CLV. HSA was incubated with CLV or CLV-B and the purified resulting conjugates were characterized by MALDI-TOF MS. Sera were incubated with CLV-B and proteins separated by 2D electrophoresis, running two gels in parallel. First gel was transferred and biotinylated proteins were detected with streptavidin-HRP. The second gel was used for total proteins detection by Coomassie staining and spots of interest were excised, digested with trypsin and identified by peptidic fingerprint. Competition experiments between CLV and CLV-B for HSA haptenation were analyzed using SDS-PAGE techniques and streptavidin-HRP for detection.

Results: MALDI-TOF analysis of conjugates showed that HSA was modified by both CLV and CLV-B (as confirmed by mass increment the protein after drug incubation). Serum proteins identified as candidate targets of CLV-B in 2D-electrophoresis were HSA, haptoglobin and heavy and light chains of immunoglobulins. As result of competition experiments, HSA pre-incubation with an excess of CLV moderately reduced the incorporation of CLV-B.

Conclusion: CLV-B is a valuable tool for the identification of CLV targets with high sensitivity. Further structural information on the binding sites on targets would elucidate potential antigenic determinants and get insights into the activation of the immune system by CLV.

TP1410 | Myeloid dendritic cells and monocyte-derived dendritic cells exhibit a different maturation pattern in patients with immediate allergic reactions to betalactams

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Background: The analysis of maturation of Dendritic Cells (DCs) is a useful *in vitro* assay to analyze their specific response to Betalactams. Many studies use monocyte-derived Dendritic Cells (moDCs) instead of myeloid DCs (mDCs) because of the low number of the later in blood. Although this approximation is well validated, moDCs are more similar to monocyte than from DCs. Therefore, the main objective of this study was to analyze the maturation and activation differences between mDCs and moDCs in the recognition of Amoxicillin (AX) and Clavulanic acid (CLV).

Method: mDCs and monocytes were isolated from peripheral blood mononuclear cells (PBMCs) from 10 allergic patients with selective immediate allergic reaction to AX, CLV and from 10 controls. moDCs and mDCs were cultured with the culprit drug. Expression of CCR7, CD40, CD80, CD83 and CD86 markers were analyzed by flow cytometry and represented as Maturation Index (MI).

Results: Higher expression of maturation and activation markers were detected in cells from allergic patients compared with controls. Higher MI of CCR7, CD40 and CD86 were found in mDCs of allergic patients to AX compared with moDCs ($P = 0.006$, $P = 0.02$, $P = 0.02$) respectively. Moreover, higher MI of CCR7 ($P = 0.04$) and CD40 ($P = 0.01$) were found in mDCs of CLV allergic patients. No differences were found in CD80 and CD83 expression.

Conclusion: The analysis of maturation and activation shows higher MI when use mDCS, suggesting that the use of mDCs could represent a more realistic and accurate approximation to the biological process.

TP1411 | Positive drug provocation test to amoxicillin in patients with negative skin test

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Background: Betalactam antibiotics (BL) are one of the main causes of drug hypersensitivity in Spain, being amoxicillin the most involved in our country. For diagnosis, sensitivity of skin tests is not 100%; therefore, drug provocation test (DPT) is necessary.

Method: We described clinical characteristics of 50 patients with confirmed immediate reaction to a BL compound, negative skin tests and positive DPT to amoxicillin. For descriptive analysis, patients were classified in 2 groups according to symptoms reported in clinical history: Group 1, patients with anaphylaxis and Group 2, patients with urticaria. Symptoms and median cumulative dose (MCD) for positive DPT, interval of time between allergic reaction-DPT and between DPT drug intake-positive DPT were analysed.

Results: In group 1, 23 patients were included and 27 in group 2. Patient median age was 41.14 (15-76) year-old and 64% female. BL implicated were amoxicillin 19 (38%), amoxicillin-clavulanic 23 (46%), Penicillin 5 (10%), Cefazoline, Cefuroxime and Cefalexine 1 (2%) respectively. During DPT 16 patients (32%) developed anaphylaxis, (12 from Group 1 and 4 from Group 2), and 34 (68%) urticaria (11 from Group 1 and 23 from Group 2). Group 1 reacted to 170.4 mg of AX in DPT and group 2 to 233.7 mg ($P > 0.05$). Patients of group 2 reacted after a longer period of time for positive DPT than group 1, median 15 minutes (15-30) vs 30 minutes (15-60) (P 0.01).

Conclusion: DPT is the most important tool for drug hypersensitivity diagnosis and it is necessary despite negative skin test. Lower doses and less time are necessary for positive DPT in patients with anaphylaxis. The severity of the symptoms developed in the BL allergic reaction did not determine the response in the DPT.

TP1413 | Drug provocation tests with Beta-Lactams and re-exposure rate

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Background: Most referrals of suspected antibiotic allergy with non-immediate hypersensitivity reactions (NIHSR) in children are due to beta-lactams (BL). Drug provocation tests (DPTs) are the gold-standard method to rule out this important diagnosis, but standardization of DPTs is required. The optimal duration of the drug intake is still unestablished, and protocols range from one to several days. Our study's purpose was to compare the BL re-exposure rate after a DPT using two different protocols (one-day, or short protocol, versus 3-7 days, extended protocol), in diagnosing NIHSR with BL in children followed at our outpatient clinic.

Method: Using a questionnaire performed after a negative DPT with a BL, we analyzed the frequency of re-exposure rate to the tested drug according to the two protocols: short (one-day) and extended (3-7 days) DPTs.

Results: Sixty-one patients were included (38 were males). The median age at the time of the reaction was 3 years (P25-P75: 1-4 years) and age at the time of the DPT was 4 years (P25-P75: 2-6 years). All the reactions were mucocutaneous. The implicated drugs in the reaction were: amoxicillin in 31 patients, amoxicillin-clavulanate in 27 children, and cephalosporins for the remaining three. Thirty-four (57%) children performed a short DPT and 27 an extended DPT. The time delay between the reaction and the DPT was slightly higher for those that underwent an extended DPT (P-value = 0.023). Thirty-six (59%) children were re-exposed to BL months to years after the negative DPT. Children that performed a short DPT presented a higher re-exposure rate than the ones that performed an extended protocol (71% versus 44%, P-value = 0.039).

Conclusion: An important proportion of the children that underwent a DPT did not take any BL after the test, particularly those that performed an extended protocol. The reasons are unclear but psychological factors like resistance in accepting new provided evidence that conflicts with personal beliefs and the consequential increase of the last ones, may have contributed.

TP1414 | Positive skin test with clavulanic acid – our experience

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Background: The betalactam antibiotics (BL) are one of the most frequently used antibiotics. Clavulanic acid (CLV) is a BL with weak antibacterial activity but due to its betalactamase inhibition is used in combination with amoxicillin.

Skin prick test (SPT), intradermal tests (IDT) are very important in the diagnosis of drug allergy. A drug provocation test (DPT) is often needed in order to diagnose drug hypersensitivity reactions. CLV is available in Spain only in combination with amoxicillin, which complicates further potential testing with this drug.

The objective of the study was to compare the skin test (ST) positive for CLV with the diagnostic of allergy to CLV.

Method: We review the positive ST with CLV in our drug unit between 2017 and 2018. We performed SPT and IDT with reagents provided by DIATER Laboratories (Diater Madrid, Spain). The

concentration used for SPT was 20 mg/mL and for IDT were the following: 0.5 mg/mL, 5 mg/mL and 20 mg/mL. After obtaining informed consent we performed DPT according to the skin test. We also performed DPT in all patients with positive non-immediate IDT.

Results: 32 patients had positive ST with CLV. 12 patients need more tests to finish the study. From the 20 patients that ended the study there were 31 ST positive with CLV (we re-evaluated some of the patients 1 month after). SPT and IDT with the concentration of 0.5 mg/mL was negative in all of the cases.

The 5 mg/mL IDT was positive in 6 cases, 1 immediate (diagnose of CLV allergy) and 5 non-immediate (negative DPT, excluding allergy diagnosis).

The 20 mg/mL IDT was positive in 25 cases, 5 immediate and 20 non-immediate. In all the positive non-immediate IDT 20 mg/mL the DPT was negative (excluding allergy diagnosis).

From the 5 positive immediate IDT 20 mg/mL in 3 cases the DPT was negative (excluding allergy diagnosis). In 2 tests (from the same patient) the allergy diagnose was made.

Conclusion: In our study we found that non-immediate positive CLV IDT might have a low sensibility. More study are necessary to improve the value of ST with CLV.

TP1415 | Allergy tests in pregnant women with syphilis and history of penicillin allergy in Brazil

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Background: Benzathine penicillin is considered the only effective drug in the treatment of congenital syphilis. The increase in the prevalence of syphilis in pregnancy has increased the demand of reference centers in the investigation of penicillin allergy in Brazil. *Objective*: To describe associated factors with history of penicillin allergy and results of tests and desensitisation of pregnant women with syphilis treated at the Allergy and Immunology outpatient clinic in University Hospital of Federal University of the State of Rio de Janeiro.

Method: Sixty one pregnant women with syphilis and a history of penicillin allergy were included. Information on allergic reactions and skin tests was obtained, and when negative and when there were nonspecific symptoms, oral provocation test was performed with oral Penicillin. Desensitization was indicated in the other cases.

Results: A total of 61 patients were included, mean age was 26.81 ± 7.84 years old, mean gestational age was 16.06 ± 9.07 years. The mean age of the reaction was of 17.94 ± 10.44 years and mean time between reaction and care was of 9.16 ± 9.89 years. 85% had a history of Benzathine Penicillin reaction, the remainder to amoxicillin and oral penicillin. 46% had a history of immediate reactions including anaphylaxis, 31% late reaction, and 23% undetermined. 10% had a history of a local reaction, 15% had non-specific reactions, 4.5% presented a suspected Jarisch Herxheimer reaction and the remaining skin and / or respiratory reactions. The cutaneous test with potassium penicillin G was positive in two cases, including one patient with a history of late reaction and none reacted to oral provocation test. Eleven patients were desensitized based on the positive cutaneous test and recent history of immediate, specific reaction according to Wendel's protocol. One patient with positive test and late reaction had a mild reaction during desensitization. All patients completed treatment

Conclusion: The skin test appears to be safe in pregnant women and predictor of immediate allergic reaction to Penicillin; however, it should be done independent of the time interval between administration and reaction.

TP1416 | Basophil activation test (BAT) is a useful tool for the diagnosis of drug allergy: A case report

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Case Report:

Background: B-lactams are considered frequent causes of immediate drug reactions. Approximately 20% of drug related anaphylaxis deaths in Europe are caused by penicillin. Skin testing (ST) to β-lactams is a useful tool for the assessment of β-lactam allergic patients due to its high negative predictive value.

Method: We report the case of a female, 26-year-old patient who had a history of anaphylaxis after iv administration of cefuroxime. The reaction had taken place two months before her visit to our department. She had received β-lactams, including cefuroxime, in the past without any allergic symptoms. The patient also suffered from allergic rhinitis, asthma and food allergy (LTP syndrome). Written informed consent for publication has been obtained from the patient. SIgEs to β-lactams (ImmunoCAP C1, C2, C5, C6, C7) and to latex (K82) were measured and all were negative (<0.1KU/L). Base Tryptase was also low (3.1 ng/mL). Subsequently, skin prick tests (SPT) and intradermal tests (ID) to PPL, MDM, penicillin, amoxicillin, ampicillin, cefuroxime, imipenem, meropenem and aztreonam were performed. All the STs were negative except for the ID to amoxicillin and ampicillin (concentration 20 mg/mL), in which the wheal diameter was less than 3 mm greater than the negative control (and thus could not be considered positive), but flare was evident. STs were performed twice for the confirmation of the initial results.

Results: As the results of the STs were not in accordance with the clinical history of anaphylaxis to cefuroxime, it was decided to perform BAT to amoxicillin and cefuroxime. The BAT was positive to both amoxicillin and cefuroxime. Based on the clinical history of anaphylaxis and in the positive BAT, we advised our patient to avoid all β-lactams and in case a β-lactam antibiotic is needed, it should be given by a desensitization procedure.

Conclusion: During the last decade, in our department, more than 2000 patients underwent STs to β-lactams. It was the first time that the inconsistency of clinical history and STs results led us to ask for a BAT. In our case, BAT has been proven to be a useful tool for the management of a patient whose STs results were inconclusive.

TP1417 | Beyond the antimicrobial sulfonamides

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Case report: We present a case of a 70-year-old male, with a history of atrial fibrillation, dyslipidemia, obesity and chronic kidney disease stage 4. He was admitted at Nephrology department for maculopapular purpuric lesions that appeared one month ago in lower limbs with extension to buttocks, trunk and upper limbs. Those lesions were also pruritic and didn't disappear with pressure. The patient related that symptomatology after taking least one week furosemide at a dose of 80 mg a day, and improved when the drug was removed. 10 days after the replacement of the diuretic treatment with 10 mg of torasemide a day, the lesions reappeared accompanied by fever (38°c) and macroscopic hematuria. There were no signs or symptoms of infection in the initial assessment. During the hospitalization, skin and kidney biopsies were performed, both compatible with leukocytoclastic vasculitis. The patient referred for many years supposed edema in hands with a sulfonamide without specifying more data, although in his medical history he had taken furosemide 40 mg and celecoxib repeatedly.

Materials and methods: After our evaluation, we performed prick with torasemide 10 mg/mL; Intradermal tests with furosemide (1 mg/mL), trimethoprim (16 mg/mL) sulfamethoxazole (100 mg/mL) and epicutaneous tests with furosemide, torasemide and trimethoprim-sulfamethoxazole (in petrolatum 10%) with late reading at 72 hours. Finally, we performed oral exposure test with spironolactone, trimethoprim-sulfamethoxazole and furosemide.

Results: Prick, intradermal and epicutaneous tests were negative (negative control patients). Subsequently, the oral exposure test with spironolactone 25 mg had good tolerance but with trimethoprim-sulfamethoxazole (80/400 mg), 6 hours later the intake, pruriginous macules measuring 2x3 cm appeared on the back of both hands (similar reaction the patient reminded with taking sulfonamides years ago), and with furosemide 40 mg, after 36 hours, painful, erythematous plaques measuring 6x5 cm appeared in both legs and right cheekbone.

Conclusion: We present the clinical case of a patient with hypersensitivity vasculitis after taking non-antibiotic sulfonamides and fixed exanthem by trimethoprim-sulfamethoxazole, whose diagnosis was confirmed by the clinical history, histological findings and allergological exploration. Although sulfonamide allergy has been described, the cross-reactivity between antibiotic and non-antibiotic sulfonamides is considered exceptional.

TP1418 | Hypersensitivity to multiple corticosteroids: A challenging work-up

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Case report: Corticosteroids (CS) are widely used for their anti-inflammatory effects. As corticosteroids are often used to treat allergic reactions, they can be overlooked as a cause of immune-mediated hypersensitivity reactions (HS). However, allergic reactions to CS have been reported with an estimated prevalence of 0.1 to 0.3%, being the delayed type reactions to topical CS more frequent than the immediate-type.

A 42-year-old woman presented with a history of several episodes of HS to the administration of endovenous and topical CS. The first episode occurred during adolescence, with facial angioedema following the administration of an unknown endovenous CS. The second episode occurred in her 20's, also with facial angioedema following the administration of intranasal CS (budesonide). More recently, she had experienced late contact dermatitis after manipulating her son's intranasal CS (fluticasone furoate, mometasone furoate and beclomethasone). She also has a non-atopic persistent rhinitis and does not tolerate any nasal CS. Skin prick tests (SPT) and intradermal tests (ITD) with CS (prednisolone, methylprednisolone succinate, hydrocortisone succinate, dexamethasone phosphate, betamethasone) and latex were negative, including immediate and late readings. We decided to do an oral drug challenge with deflazacort (total dose 33 mg) that was positive – generalized erythematous reaction and palpebral edema 3 h after administration. A month later we performed a drug challenge with endovenous dexamethasone (5 mg) and later with oral betamethasone (5 mg), both negative. We performed patch tests with the CS present in the GPEDC (Grupo Português de Estudo das Dermatites de Contacto) portuguese baseline series (budesonide and hydrocortisone butyrate) as well as with the available nasal CS (fluticasone furoate and budesonide). At the 48 h reading, the patch test was strongly positive to budesonide and after 96 h it was positive to all CS tested.

This case illustrates the challenging management of CS allergy. HS to deflazacort was confirmed but we were not able to identify the culprit of EV CS reaction. We found tolerated options for systemic administration (oral and ev), but still haven't found a nasal CS that can treat what the patient needs the most, her non-atopic rhinitis. Written consent to share clinical information was given by the patient.

TUESDAY, 4 JUNE 2019
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MANAGEMENT OF DRUG HYPERSENSITIVITY

TP1419 | Meloxicam could be administered safely in two equal doses, during open oral challenge in patients with nonsteroidal antiinflammatory drugs hypersensitivity

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Background: Nonsteroidal Antiinflammatory Drugs Hypersensitivity (NSAIDs-H) is common in general population. Imbalance between enzymes COX-1 and COX-2, has been postulated as the principal mechanism for NSAIDs-H. Previous studies have shown that the selective COX-2 inhibitor meloxicam, is an effective and safe option in patients with NSAIDs-H. Our aim was to evaluate if meloxicam could be administered safely in two steps, until completion of the therapeutic dose, during open oral challenge.

Method: Patients with history of NSAIDs-H (presence of cutaneous and/or respiratory symptoms with one or more conventional NSAIDs or meloxicam) were included. Everyone underwent an open oral challenge with meloxicam in two steps of 5 and 10 mg, or 7.5 and 7.5 mg (total cumulative dose of 15 mg). Placebo was not used at the beginning of the procedure. The time interval between both doses was 45 minutes. Spirometry, pulse oximetry and vital signs were recorded at onset, at the moment of the second dose (45 minutes), 60 and 180 minutes after the last dose. At the moment of discharge, instructions regarding delayed reactions were given. Informed consent was obtained for each patient. Information was taken from the data base of allergology unit at Fundación Valle del Lili.

Results: One hundred ninety nine patients were analyzed, 25 of them (12.6%) had between 12 and 18 years of age, 143 (72%) were female. Forty eight percent underwent the challenge receiving 5 and 10 mg and 52%, 7.5 and 7.5 mg. The challenge was negative in 187 (94%). There was no difference in tolerance between those receiving a minor dose (5 mg) in the first step and those receiving 7.5 mg.

Conclusion: Oral challenge with two equal doses of meloxicam in patients with NSAIDs-H, seems to be equally safe and probably undergoes less costs and less time spend, making it easier to perform in routine clinical practice.

TP1420 | Anaphylaxis after successful desensitization to glatiramer acetate

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Case Report:

Background: Glatiramer acetate (GA; Copaxone, Teva Pharmaceuticals) an immuno-modulatory drug used as a first-line treatment in relapsing-remitting multiple sclerosis (MS). Reducing relapse frequency and preventing disease progression. Nevertheless, there are some cases of anaphylaxis reported, even after prolonged treatment. Literature reinforces desensitization as an effective therapeutic procedure in hypersensitivity reactions (HSR) related to GA.

Objective: Report a case of GA anaphylaxis after a successful desensitization.

Methods: Skin prick test (SPT) for GA: 2 and 20 mg/mL, intradermal (ID) tests: 0.002, 0.02 and 0.2 mg/mL and basophil activation test (BAT): 0.001, 0.1, 1 mg/mL. Desensitization was performed administrating SC GA doses every 30 minutes up to 20 mg/dl.

Results: A 49 year-old woman with no atopic background and MS diagnosis treated for 1.5 year with SC GA 20 mg, 3 days/week without local reactions and adequate disease control. Attended the emergency room (ER) due to cutaneous and abdominal symptoms developed 15 minutes after the administration of GA. No respiratory or hemodynamic compromise. Treatment with IV steroids and antihistamines was initiated and discharge was held after 8 hours of observation. Serum tryptase: 20.2 μg/L. Total IgE: 279 kUA/L. Normal blood count and hemostasis.

The allergy evaluation was performed 8 weeks after the episode. Baseline tryptase: 6 μg/L, SPT were negative for GA, food allergens and Anisakis. BAT with GA was positive and negative in 2 healthy controls. The patient gave informed consent to perform a desensitization. Increasing SC doses of GA were administered up to 23 mg. The procedure lasted over 2 hours and was well tolerated. Initial tryptase: 7 μg/L, remained invariable after the procedure. Habitual doses of GA were reintroduced with no recurrence.

After 1 month a second anaphylaxis episode (cutaneous, respiratory and abdominal compromise) motivated another ER visit. Symptoms resolved with similar treatment. Tryptase was not evaluated. Therapy with GA was discontinued. Five months later a second BAT was performed resulting positive (C-: 3.06%, GA: 8.47% IE: 2.76).

Conclusions: HSR to GA may develop at any time during MS treatment. Desensitization to GA allows to continue therapy in case of allergic sensitization. However, continuous medical follow-up must be provided, even after GA tolerance is confirmed. BAT is a useful tool when skin tests are negative and specific IgE is not available.

TP1421 | Successful desensitization of a patient with IgE-mediated anaphylactic reaction to FVIII/VWF concentrate

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Case report:

Background: Type 3 von Willebrand disease (VWD) is a severe bleeding disorder with a prevalence of 1:1million live births. There are several von Willebrand factor (VWF) replacement products used in the treatment of acute bleeding episodes or as prophylaxis. Patients who receive multiple transfusions have an increased risk of developing antibodies against these products. These antibodies can lead to life-threatening anaphylactic reactions. Previous studies have identified immune complex formation and complement activation as the trigger for anaphylaxis, rather than IgE. IgE-mediated anaphylaxis against VWF concentrates has not yet been published.

Case: A four-year-old female patient with type3 VWD was referred to our hospital because of an anaphylactic reaction during FVIII/VWF concentrate infusion. She had previously received FVIII/VWF concentrate infusions eight times without any complications. She did not have antibodies against VWF and FVIII, and serum IgA level was normal. Since she needed factor replacement therapy as a result of a growing hematoma on her scalp, we performed skin prick and intradermal tests two days after the reaction. The prick test, with FVIII/VWF, was negative, but the intradermal test was positive. We administered a twelve-step desensitization protocol with FVIII/VWF concentrate successfully without any reactions.

Conclusion: Anaphylactic reaction to factor replacement products is a major problem for patients with VWD, especially type3 VWD requiring multiple factor infusions. We achieved a successful desensitization with FVIII/VWF concentrate in a patient who had an anaphylactic reaction during the infusion of this product. Our patient is important since she represents the first case of IgE-mediated anaphylaxis against VWF concentrate reported in the literature.

TP1422 | Evaluation of safety and tolerance of desensitization to platin salts and taxanes

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Background: The increasing use of platin salts (PL) and taxanes (TX) has led to a rise in hypersensitivity reactions (HR), which compromise their use as first-line therapy. Desensitization (DS) can be an option in patients with HR to PL and TX, avoiding the use of less effective treatments, although reactions can occur.

Method: Retrospective analysis of medical records from DS to PL and TX performed in our department (2014-2018). Safety and tolerance of this procedure were analyzed. DS protocols were tailor made considering the severity of reaction and the results of skin tests (ST).

Results: A total of 149 DS were performed: 83% (n = 124) to PL, 17% (n = 25) to TX, corresponding to 32 patients (66% female; median age 57.2 years [33-73]). Protocols were tailor made using 1-4 bags/ 8-19 steps, mean of DS per patient 4.53 (SD 3.8).

DS to PL included oxaliplatin (77%), carboplatin (18%) and cisplatin (5%). Anaphylaxis was the most common initial reaction (54%), followed by cutaneous symptoms (42%). ST were positive in 65% patients (71% IDT, 29% SPT). Reactions during DS to PL occurred in 10% (n = 12), corresponding to 7 patients (cutaneous 78%; anaphylaxis 11%; chills 11%). These reactions occurred with < 10% of the target dose in 4 DS, 10-20% in 4, 40-50% in 2, 50-60% in 2; 11 of them were mild and less severe than the initial reaction; one was more severe. Four patients had reaction in the first DS, 2 after step reduction. Only 1 patient did not continue DS because of persistent reactions during the procedure; the remaining achieved the target dose. Occurrence of reactions was not associated with ST positivity ($P = 0.443$).

DS to TX included docetaxel (68%) and nab-paclitaxel (32%). Anaphylaxis was the most common initial reaction (67%), followed by flushing and back pain (33%). ST were positive in 50% (all IDT). No reactions occurred during DS to TX.

Conclusion: Reactions during DS to PL and TX can occur in up to 20% but are usually mild and less severe than the initial reaction. In our population, reactions occurred in 8% of all DS, only with PL and 92% were mild. Most of the patients (n = 31) were able to achieve the target dose. Thus, our results support the safety and tolerance of DS to PL and TX.

TP1423 | Successful desensitization to oxaliplatin using omalizumab: A case report

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Case Report:

Background: Omalizumab has been used as adjuvant therapy for achieving desensitization to allergens such as cow milk and hymenoptera venom. Only a few cases of pre-treatment with omalizumab in situations of failed desensitization to platinum-based drugs have been reported. The purpose of this case report is to share our experience in achieving a successful desensitization to oxaliplatin (after initial failure) by adding omalizumab to an 18-step protocol.

Case summary: A 57-year old patient diagnosed with metastatic sigmoid adenocarcinoma was initially treated in 2014 with 6 folinate, oxaliplatin, 5-fluorouracil and bevacizumab cycles followed by 3 more cycles after 5 months. In 2016 he received 2 additional cycles, and presented with an anaphylactic reaction during the second one, with positive skin testing to oxaliplatin. An attempt was made to substitute oxaliplatin with irinotecan; he presented with anaphylaxis and positive skin testing to this drug as well. In 2018, due to cancer progression, he underwent an oxaliplatin 12-step desensitization, which was suspended after another severe hypersensitivity reaction at a threshold dose of 7 mg. At this moment, a total IgE level of 7410 kU/L was documented. Despite extending the desensitization protocol to 16 steps, the patient presented with anaphylaxis in a second attempt that was run 48 hours later. In agreement with the patient and the oncology department, a 300 mcg dose of subcutaneous omalizumab was administered. A provocation test with acetylsalicylic acid was conducted – he had a history of possible NSAID hypersensitivity - and 300 mcg were added to his premedication plan. Two weeks after anti-IgE treatment, he successfully tolerated an 18-step oxaliplatin desensitization. The procedure was repeated every two weeks for the subsequent 4 cycles, using 300 mcg of omalizumab two weeks before each cycle, and both montelukast and AAS as premedication. No new hypersensitivity events occurred, and the patient achieved radiological remission stability of cancer.

Conclusions: The use of adjuvant omalizumab after each desensitization was successful in allowing the completion of all subsequent oxaliplatin cycles in a patient with previous failed desensitizations.

Keywords: Desensitization, Omalizumab, Oxaliplatin, Drug allergy.

TP1424 | Failure of adjuvant omalizumab in drug desensitization

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Case report: There is a well-recognized surge in the prevalence of hypersensitivity reactions (HSR) to chemotherapeutic agents. Desensitization protocols enable keeping on first-line drugs despite HSR. However, in a few cases, desensitization is not tolerated. In the aforementioned scenario, adjuvant use of omalizumab has been proposed. We present 2 cases of failed drug desensitization in spite of using omalizumab.

CASE 1: a 58-year-old male with rectal adenocarcinoma (2014) received 7 chemotherapy cycles (oxaliplatin-capecitabin). Disease progression required a treatment change twice (2016: cetuximab-folfiri; 2018: folfox).

During the infusion of oxaliplatin (7th cycle, 2015) he presented facial pruritus, dyspnea, oxygen desaturation (70%), BP 70/30 mmHg, HR 120 bpm, followed by decreased level of consciousness and bradycardia, requiring epinephrine. Prick-test to oxaliplatin (5 mg/mL) was positive. In 2018 oxaliplatin was reintroduced. First desensitization with a 16-step protocol using dexchlorpheniramine, ranitidine, montelukast and salicylic acid as premedication, was well tolerated. Second desensitization was withdrawn after suffering facial erythema and oxygen desaturation (88%) twice, at protocol-steps 7 and 8 (tryptase 44.7 mcg/L 1 hour later). A third attempt adding omalizumab 300 mg 6 days before desensitization was unsuccessful developing the same symptoms at step 1 (tryptase 14.5 mcg/L; 1 hour).

CASE 2: a 78-year-old male with chronic ischemic cardiomyopathy, diagnosed with a MALT-lymphoma, was started on bendamustine-rituximab. First cycle was completed despite the development of urticaria. The second cycle was withdrawn due to generalized urticaria, profuse sweating, hypotension 60/40 mmHg and confusion. Intradermal test to rituximab (10 mg/mL) was positive. A first desensitization using a 16-step protocol, after methylprednisolone, dexchlorpheniramine, ranitidine, montelukast and salicylic acid, was not completed because urticaria appeared three times at step 16. Two doses of omalizumab 300 mg were administered 14 and 3 days before next desensitization, but generalized urticaria appeared again at step 16. The patient refused to continue.

Omalizumab has shown to improve tolerance and security of several allergologic therapeutic procedures, including drug desensitization. However, its use is not always successful as shown in these 2 patients. Further studies are needed to find predictive factors for its successful use.

TP1425 | Successful high risk oxaliplatin desensitization using omalizumab

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Case report:

Background: Human anti-IgE (Omalizumab) has been successfully used to improve severe asthma and chronic urticaria. Recent studies have shown its utility in food desensitization protocols and Hymenoptera venom immunotherapy in highly sensitized patients. The use of omalizumab in drug desensitization in highly IgE-sensitized patients needs further exploration.

Methods: A 60 years old woman with colon cancer was evaluated after a severe anaphylactic reaction to oxaliplatin. Desensitization with a 4 bags-16 steps protocol induced anaphylaxis. Two doses of Omalizumab were administered before next desensitization.

Results: During the 7th-lifetime oxaliplatin exposure the patient presented generalized pruritus, erythema, dizziness, hypotension,

and oxygen desaturation. Her tryptase was significantly elevated at 6.43 mcg/L, (baseline 1.39) and total IgE > 5000 IU/mL. Prick testing (5 mg/mL) was positive. A 16-steps desensitization protocol in the ICU induced erythema and hypotension at step 12 (cumulative oxaliplatin dose of 0.858 mg; target dose of 108 mg) requiring intramuscular epinephrine. Tryptase level 30 min into the reaction was 28 mcg/L. Due to the high sensitization to oxaliplatin, the patient received Omalizumab at 600 mg, 2 weeks before and 300 mg, the day before the next desensitization. The patient had a mild reaction with tryptase of 9.93 mL/L. Omalizumab treatment was continued before subsequent desensitizations and she tolerated four more infusions without reactions and baseline tryptase.

Conclusions: We report the use of omalizumab in a highly sensitized oxaliplatin allergic patient before desensitization. Keeping cancer patients in their first-line therapy is critical for their prognosis and quality of life. Omalizumab is a promising tool as an adjuvant pretreatment to improve the safety of drug desensitizations, providing protection from anaphylaxis.

TP1426 | Safety and efficacy of desensitization to the platinum-containing compounds

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Background: Platinum salts are strong inducers of IgE-mediated Hypersensitivity Reactions (HSRs), with oxaliplatin (Ox) being the most immunogenic. Desensitization allows to maintain the first line treatment, but HSR can also be triggered during this procedure. We analyzed the efficacy and safety of desensitization to platinum salts in a series of patients at the General University Hospital of Alicante, in the period March-December 2018

Method: Fifteen patients with initial platinum HSR were included: 10 (66.7%) with Ox (Severity: 1 grade I, 6 grade II and 3 grade III); 4 (26.7%) with Carboplatin (Cb), (1 grade I, 1 grade II and 2 grade III) and 1 (6.7%) with Cisplatin (Cis), (grade III). Skin tests with dilutions of Ox, Cb and Cis provided by the Pharmacy Service, were performed in all patients, with 12 (80%) positive results (9 Ox and 3 Cb). Desensitization procedures were carried out following previous publications (Dr. Castells, 2008).

Results: 51 desensitizations were performed in 15 patients, and 17 (33.3%) reactions were observed, in all cases the therapeutic doses could be completed. 39 (76.5%) were done with Ox, observing 15/39 (38.5%) reactions (11 grade I, 4 grade II and no grade III), with elevated tryptase in only two cases (1 grade I, 1 grade II). On the other hand, 12 (23.5%) were performed with Cb and 2/12 (16.7%) reactions were observed (1 grade I, 1 grade II and no grade III). No immediate or delayed severe HSR were observed.

Conclusion: IgE-mediated sensitization to Platinum-containing compounds was demonstrated in 80% of cases of our sample. The overall efficacy of desensitization was 66.7%, being of 61.5% for Ox and 83.4% for Cb. Patients sensitized to Ox seem to be at higher risk of developing a HSR before and during desensitization. This study confirms the importance of skin testing to establish the risk of a HSR before deciding how to re-expose patients to platinum.

TP1427 | Rapid drug desensitization for platinum-based chemotherapy drugs significantly increases peripheral blood IL-10 levels

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Background: The mechanism of rapid desensitization in immediate drug hypersensitivity is not fully understood and knowledge is mostly depending on diminishing of mast cell degranulation. We aimed to investigate the effects of rapid desensitization on peripheral blood cytokine levels in patients who had experienced immediate hypersensitivity reactions due to platinum-based chemotherapy drugs.

Method: Ten patients who had experienced immediate hypersensitivity reactions due to platinum-based chemotherapy drugs, 10 patients who were known to tolerate these agents and 5 healthy controls were included in the study as the patient group, the patient-control group and the healthy control group, respectively. Skin prick and intradermal tests with culprit agents were performed in the patient group. Serum levels of IL-4, IL-5, IL-10, IFN-g and TGF-β were analyzed by ELISA and Luminex assay [ag1] . Blood samples were collected before and 24 hours after the first, second and the last desensitization protocols in the patient group, before and after the first chemotherapy in the patient-control group and randomly in the healthy controls.

Results: The culprit agents were carboplatin in 7 patients, cisplatin in 2 patients and oxaliplatin in one patient. The patient group contain 10 female; the patient-control group contain 6 female, 4 male and the healthy-control group contain 3 female, 2 male patients. The average ages of the patient group, patient-control group and the healthy control group were 53.5 ± 4.66, 64.2 ± 5.48 and 34.6 ± 2.22 years, respectively. In the patient group, serum IL-10 levels increased significantly after the first and the last desensitizations when compared to their initial levels (*P*:0.013; *P*:0.028, respectively) and IL-10 levels were much higher after the last desensitization when compared to the basal levels measured before the first desensitization (*P*:0.044). Regarding other cytokines no relations were observed within and

TABLE 1. Longitudinal comparison of cytokine levels before and after desensitizations

	Before the 1st chemotherapy Median/ min-max	After the 1st chemother-apy Median/ min-max	P1*	Before the 2nd chemotherapy Median/ min-max	After the 2nd chemo-therapy Median/ min-max	P2**	Before the last chemotherapy Median/ min-max	After the last chemotherapy Median/ min-max	P3***	P4****
IL-4	0.13/0.13-1.42	0.13/0.13-1.72	NS	0.13/0.13-1.42	0.23/0.13-1.72	NS	0.13/0.13-1.42	0.23/0.13-0.36	NS	NS
IL-5	3.29/1.85-7.39	3.29/1.85-7.39	NS	3.29/3.29-5.13	3.29/3.29-79.81	NS	3.29/3.29-5.13	3.29/3.29-5.13	NS	NS
INF-y	0.69/0.69-8.70	0.69/0.36-8.70	NS	0.95/0.69-5.34	0.95/0.69-15.27	NS	0.66/0.66-1.69	0.69/0.69-3.04	NS	NS
IL-10	0.66/0.45-3.60	1.69/0.66-4.32	0. 013	0.89/0.66-12.01	1.29/0.66-35.11	NS	2.69/0.69-6.33	3.71/0.45-52.44	0.028	0.044
TGF-B	223.63/150.3-320.3	207.8/163.7-630.3	NS	240.3/155.30-397	217/158.7-15.27	NS	202.00/148.7-288.7	215.30/180.30-297.0	NS	NS

* Before and after the first desensitization.
** Before and after the second desensitization.
*** Before and after the last desensitization.
**** Before the first and after the last desensitization.

TABLE 2. Data of patients

	N (%)	
Culprit agent		
Carboplatin	7 (70)	
Cisplatin	2 (20)	
Oxaliplatin	1 (10)	
Reaction type		
Anaphylaxis	5 (50)	
Urticaria	1 (10)	
Angioedema	1 (10)	
Asthma	—	
Urticaria-Angioedema	3 (30)	
Reaction during desensitization		
Yes	1 (anaphylaxis)	(%30)
	2 (urticaria)	
No	7 (70)	
Skin test with culprit agent		
Positive	7 (70)	
Negative	3 (30)	
Result of desensitization		
Successful	10 (100)	
Unsuccessful	0 (0)	

between the groups. No correlations were found between the number of desensitizations and the levels of cytokine levels (Table 1).

Conclusion: IL-10 levels significantly increased after successful rapid drug desensitization but a longitudinal effect on cytokine levels with the increasing number of desensitizations could not been shown. Further studies are needed to evaluate the origin of elevated cytokines.

TP1428 | Desensitization of intravenous cyclosporine induced anaphylaxis

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Case report: Desensitization is the induction of temporary unresponsiveness to the allergen. It is effective procedure to IgE-mediated reaction in principle, and other immune-mediated reactions in some cases. A few cases of intravenous (IV) cyclosporine (CsA) hypersensitivity have been reported since 1984, is known as non-IgE mediated hypersensitivity to polyoxyethylated castor oil not to CsA itself. Oral CsA is wonderful substitute because it has no polyoxyethylated castor oil. A 18-year-old patient with graft versus host disease who suffered from IV CsA induced anaphylaxis should be administered parenteral form due to gastrointestinal trouble. We tried desensitization of IV CsA, started from 1/100 of target infusion rate, increased 1.5-2 times every hour, and successed in 10 hours.

TP1429 | Drug allergy in hematologic patient: Diagnosis and desensitization

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Background: The increasing number of oncohematologic survivors, treated with repeated courses of chemotherapy and mAbs and impaired immunologic responsiveness, is leading to an augmented drug

allergy rate in hematologic patients. On the other hand, desensitization may induce unresponsiveness to drug allergy (DA), allowing patients to be treated with life-saving medications. We propose two approaches of drug desensitization in hematologic patients, the rapid desensitization protocol, described in literature, and an allergen immunotherapy-like desensitization (AILD) protocol, both used in immediate and delayed DA.

Method: We report on: 65 patients with immediate allergic reaction to Rituximab (anti CD-20 mAb).3 patients with delayed allergy to the chemotherapeutic agent Cytarabine. 1 patient with immediate allergic reaction to Brentuximab (anti-CD30 mAb).3 patient with immediate allergic reaction to iron products (ferric carboxymaltose). For Rituximab and Cytarabine we used a 12-step AILD protocol (4 solutions with increasing concentration of the offending drug). Increasing doses of the offending drugs were administered subcutaneously. Each dose, given every second day, was fractionated into 2-4 injections, every 30 minutes. Desensitization was carried out over about 20 days.

For Brentuximab and ferric carboxymaltose we devised and implemented a 3-bag, 12-step protocol of rapid desensitization at increasing concentration, time between each step was 15-20 minutes. The total elapsed time for the procedures was about 5 hours.

Results: *Rituximab*: all patients completed the AILD without major adverse reactions. 32 patients developed late local reactions at the site of injection. After AILD, 62 patients received the planned dose of Rituximab with the previous treatment posology, without adverse reactions. However, 3 patients did not tolerate the planned dose of Rituximab.

Cytarabine: the 3 patients completed the AILD. No major adverse reactions were observed during the desensitization. Only one patient developed modest transient infiltrated nodules at the site of injection.

Brentuximab: the patient showed mild urticarial lesions during the first desensitization procedure but not during the following desensitization procedures. The drug course could be completed.

Ferric carboxymaltose: the desensitization procedure was well tolerated without adverse reactions. The drug was successfully administrated.

Conclusion: Both kind of procedures are effective, safe and can be pursued for immediate and delayed DA.

TP1430 | Rituximab-induced serum sickness disease in a patient who was desensitized for rituximab induced severe urticaria

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Case report:

Background: Rituximab is a chimeric monoclonal IgG1 antibody that binds to the CD20 molecule expressed on B lymphocytes; it has been frequently used to treat various B-cell mediated autoimmune diseases. While it is approved for the treatment of patients with rheumatoid arthritis, rituximab has also been used in off-label manner for the treatment of many other autoimmune conditions including Neuromyelitis Optica Spectrum Disorder. Early infusion-association adverse reactions are common during the first few infusions and may include a combination of fever, chills, nausea/vomiting, hypotension, bronchospasm, rhinitis, angioedema, urticaria and flushing often attributed to cytokine release syndrome associated with elevated TNF-alpha and IL-6. Late occurring infusion associated adverse reactions have been reported in a subgroup of patients receiving rituximab. These reactions may be similar to early reactions but may include additional adverse reactions such as serum sickness, SJS, TEN. We presented a case who was desensitized for rituximab induced urticaria and then developed serum sickness disease.

Case report: Four-year-old male patient with Neuromyelitis Optica Spectrum Disorder received rituximab treatment due to unresponsiveness to other treatments. At the 50th minute of Rituximab infusion administered after appropriate premedication, common urticarial reaction developed. The drug infusion was stopped. Cetirizine, montelukast, methylprednisolone were administered to the patient. It was planned to give rituximab by desensitization with family consent. During the treatment given under anaphylaxis measures, the patient did not have any urticaria, anaphylaxis, allergy symptoms. On the 12th day after infusion, the patient presented with rashes on the hands, arms and body, and on the second day, he developed fever, tenderness, pain and swelling in the joints. Laboratory tests indicated high CRP, erythrocyte sedimentation rate and low C4 levels. In the light of the history, clinical and laboratory findings, rituximab-induced serum sickness disease was considered. Antihistaminic and nonsteroidal antiinflammatory drugs were started. After the treatment, arthralgia and rashes regressed and did not recur.

Conclusion: A rare hypersensitivity reaction, serum sickness disease should be considered in patients presenting with complaints of rash, fever and arthralgia starting 1-3 weeks after treatment and should be treated without losing time.

TP1431 | Rituximab desensitization with two different protocols in two cases

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Case report:

Introduction: The frequency and severity of infusion-related reactions with rituximab have been reported in 25% -78% of patients.

Although most of the reactions were mild and moderate, serious reactions were also reported. According to the severity of the reaction, rituximab can be given to patients with different desensitization protocols.

Case1: A 7-year-old girl was diagnosed with CD27 deficiency and chronic EBV infection in pediatric oncology clinic. She tolerated the first rituximab infusion with hydroxyzine premedication. The second dose was started. After 15 min of infusion, she experienced angioedema on his eyelids and lips, vomiting, cyanotic lips and shortness of breath. She was found to be hypotensive and desaturated to 60% on pulse oximetry. The infusion was interrupted and 0.01 mg / kg intramuscular adrenaline, 1 mg / kg hydroxyzine and 1 mg / kg methylprednisolone were administered. The treatment must be continued, we decided to apply desensitization. Before desensitization, the patient was premedicated with hydroxyzine, methylprednisolone and montelukast. To date the patient has received the rituximab 4 times without any reaction with hydroxyzine premedication

Desensitization protocol: Four different dilutions were prepared (Dilution A: 0.0005 mg/mL, dilution B : 0.005 mg/mL, dilution C: 0.05 mg/mL and dilution D: 0.5 mg/m). The 13-step desensitization protocol was completed in 12.75 hours

Case2: A 7-year-old boy was diagnosed with nephrotic syndrome in pediatric nephrology clinic. He tolerated first rituximab infusion with hydroxyzine premedication. The second dose was started with hydroxyzine premedication .After 60 min of rituximab infusion, he experienced urticaria on his face. The infusion was interrupted and 1 mg / kg hydroxyzine and 1 mg / kg methylprednisolone were administered. The treatment must be continued, we decided to apply desensitization. Before desensitization, the patient was premedicated with hydroxyzine. To date the patient has received the rituximab 2 times without any reaction with hydroxyzine premedication

Desensitization protocol: Three different dilutions were prepared (Dilution A : 0.005 mg/mL, dilution B: 0.05 mg/mL and dilution C: 0.5 mg/m). The 12-step desensitization protocol was completed in 5 hours.

Conclusion: By using desensitization protocols, two patients with different clinical features have continued their rituximab therapy without complications.

TP1432 | Successful desensitization protocol to intravenous brentuximab vedotin

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Case report:

Background: Brentuximab vedotin (BV) is a monoclonal antibody drug conjugate which targets CD30. It is indicated for Hodgkin Lymphoma (HL) relapsed or after stem cell transplantation, CD30-positive non-HL and systemic anaplastic large cell lymphoma. Adverse effects include peripheral neuropathy, neutropenia, upper respiratory tract infections, gastrointestinal disorders, pulmonary toxicity, pancreatitis. In the literature, anaphylactoid reactions such as nausea, dyspnea, pruritus, pyrexia and cough occur up to 12% while few IgE mediated hypersensitivity reactions including anaphylaxis have been reported. We present a desensitization protocol to intravenous BV used in a patient for HL.

Method: A 41-year-old female with HL of nodular sclerosing subtype was referred to the Department of Allergy at Sotiria General Hospital of Athens. The patient had been treated with two cycles of VD with no adverse reactions. Then she was rechallenged with BV approximately 5 months later. After readministration of half of the total dose of VD, the patient presented flushing, pain in the oral cavity, sensation of burning in the genital area, difficulty in breathing and chest tightness. The infusion was immediately stopped and dimethindene, ranitidine, methylprednisolone and oxygen were administered with gradual recovery of symptoms. Premedication for 3 days was administered including methylprednisolone, cetirizine,

TABLE 1

Solution (mg/mL)	Rate (ml/h)	Time (min)	Volume (mL)/Dose (mg)
1 (0.0066 mg/mL)	2	15	0.50 mL/0.0033 mg
1	5	15	1.25 mL/0.00825 mg
1	10	15	2.50 mL/0.0165 mg
1	20	15	5.00 mL/0.033 mg
2 (0.066 mg/mL)	5	15	1.25 mL/0.0825 mg
2	10	15	2.50 mL/0.165 mg
2	20	15	5.00 mL/0.33 mg
2	40	15	10.00 mL/0.66 mg
3 (0.66 mg/mL)	10	15	2.50 mL/1.65 mg
3	20	15	5.00 mL/3.3 mg
3	40	360	240 mL/158.75 mg

ranitidine, paracetamol and montelukast. A desensitization protocol with BV was conducted.

Results: The desensitization protocol consisted of preparation of 3 different solutions (with concentrations of 0.0066 mg/mL, 0.066 mg/mL and 0.66 mg/mL) and the administration of total dose in 11 steps at increasing infusion rates every 15 minutes. The patient received the therapeutic dose (165 mg) with no adverse reactions. The same successful protocol was applied in subsequent infusions (Table 1). Written informed consent for publication has been obtained from the patient.

Conclusion: Monoclonal antibodies have the potential to induce adverse reactions that limit their use. Desensitization protocols are indispensably necessary for safe administration of these drugs as there is no therapeutic alternative in these patients. We hereby report a case of a patient with HL who was successfully treated with a desensitization protocol to intravenous BV.

TP1433 | Anaphylaxis and desensitization to RAMUCIRUMAB: About a first case

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Background: Ramucirumab (RCB) is a human monoclonal antibody directed against the vascular endothelial growth factor 2, produced within murin cell NS0, indicated for the treatment of gastric cancer, in association with Paclitaxel (PCL). There is not any anaphylaxis to RCB reported (1).

Method: A 53 years old man, with no medical history or any history of allergy, has been referred to the allergy unit for a grade 1 anaphylaxis, an urticaria, occurring during the first injection of RCB and before PCL. Serum tryptase was 16.6 µg/L at time 50 minutes, and 6.1 µg/L at base.

This craftsman did not report any tick bites, and was regularly hunting and eating mammal meats, including offals, without any reaction. Skin prick tests (SPT) and intradermal test (IDT) have been performed using RCB, Cetuximab (CTX) (2), Gelofusine, red meat and pork kidney. Levels of immunoglobulin E (IgE) directed against AlphaGal, and basophils activation test (BAT) for RCB, CTX and Gelofusine have been evaluated. Desensitization to RCB (3), and AlphaGal IgE inhibition tests with RCB and CTX have been proposed.

Results: IgE against AlphaGal level was 82.5 kU/L, and total IgE was 1888 kU/L. SPT : histamine 6/27 mm, control was 0 mm. IDT for RCB was doubtful at 0.5 mg/mL, IDT for CTX was positive at 0.05 mg/mL, and for pure Gelofusine. SPT were negative for Beef, Pork meat, and Pork kidneys. BAT were positive for CTX and RCB. AlphaGal IgE immunocap inhibition test was positive for CTX but not for RCB. Under premedication with methylprednisolone, Ranitidine and dexchlorpheniramine, the desensitization was performed using a one bag protocol of RCB 2 mg/mL, during 5 hours, until the dose of 8 mg/Kg, without any reaction.

Conclusion: We report the first case of anaphylaxis to Ramucirumab, and a successful desensitization protocol to this drug. Further investigations are needed to evaluate the role of AlphaGal or another carbohydrated epitope in anaphylactic reaction to this monoclonal antibody produced within murin cells.

TP1434 | Successful desensitization with panitumumab; a case report

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Case report: 60 years old male patient was diagnosed with colon adenocarcinoma and treated with adjuvant chemotherapy without an allergic reaction in a total of 8 cycles. After the disease progression, panitumumab was planned to be given. The patient was able to take the first dose without an allergic reaction. The second infusion was given smoothly, but 10 minutes after the end of infusion, the patient had diffuse urticaria, itching on the soles of the feet, mild drowsiness and these symptoms regressed with the use of feniramine and methylprednisolone. 2 weeks later, after the third infusion, the patient developed redness, itching and dizziness. Skin prick test with undiluted form of panitumumab was performed and it was negative. In 1/1000 - 1/100 - 1/10 dilutions intradermal test was performed and found to be negative. Since these results could not rule out a non-IgE-mediated reaction, desensitization with panitumumab was planned because there was no alternative treatment option for the patient. In our case, solutions were prepared at 3 different dilutions in accordance with the desensitization scheme of Castells. The patient was desensitized successfully after premedication with methylprednisolone, feniramine and cetirizine. The patient had acneiform and pustular lesions on the face and trunk before the fifth infusion and for this reason it was discussed with oncology department and decided to terminate panitutumab treatment.

Panitumumab is a complete humanized monoclonal antibody against EGFR used in metastatic colorectal malignancies. In the literature, patients who had an allergic reaction with cetuximab were reported to have successfully completed treatment with panitumumab. Fewer allergic reactions are expected with panitumumab, a fully humanized monoclonal antibody, than cetuximab, a mouse and human chimeric monoclonal antibody. The frequency of reported hypersensitivity reactions was 4%. However, in the literature 2 cases of anaphylaxis with panitumumab, desensitized with cetuximab successfully. We aimed to present our case with allergic reaction to panitumumab because of its rarity. Also this is

the first case of desensitization with panitumumab in the literature as far as we know.

TP1435 | Successful desensitisation with alemtuzumab in a relapse remitting multiple sclerosis case

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Case report:

Introduction: Alemtuzumab is a monoclonal antibody directed against CD52. Its use is permitted for relapsing remitting multiple sclerosis (RRMS). We describe a RRMS case with successful desensitization to alemtuzumab.

Case report: Our patient was a 40-year-old woman with a personal history of acute urticaria periods. Since 2008, she had received intravenous(IV) corticosteroids, IFN- beta and fingolimolid for RRMS. Due to clinical progression, changing therapy to alemtuzumab was determined. Alemtuzumab was planned to be given as an IV infusion of 12 mg/d for 5 consecutive days in the first cycle and after one year 3 consecutive days in the second cycle. At the first three days, IV dexchlorpheniramine (5 mg) and methylprednisolone (1000 mg) one hour before alemtuzumab were planned to be administered and then for the last two days, IV dexchlorpheniramine (5 mg) and methylprednisolone (100 mg) were planned for premedication. During infusion number 1, after 3.5 hours (h) of initiation, although the patient showed itchy, erythematous cutaneous eruption with a miliary pattern, despite premedication; therapy was finished completely in four hours of infusion as planned previously. On the second day, after 2.5 hours, urticaria accompanying bronchospasm and laryngeal edema were occured. She was consulted to our department, and she was assessed to have a grade 2 anaphylactic reaction (Brown grading scale of anaphylaxis). Drug skin tests could not be performed due to the premedications. Since alemtuzumab was the only therapeutic alternative, the patient underwent alemtuzumab desensitization according to a 12-step, 3 bags protocol. The patient was premedicated with montelukast (10 mg/24 h) and levosetirizine (10 mg/24 h) orally, before administration; and IV dexchlorpheniramine (5 mg) and methylprednisolone (1000 mg on the third infusion day for the remission therapy of her MS and, on the fourth and fifth days, 100 mg) one hour before starting. Totally 12 mg was administered IV during a period of 3 h. The total amount was prepared in three bags (1.-10 mL, 2.-10 mL and 3.-80 mL). Alemtuzumab desensitisation protocol was successfully completed.

Discussion: Our case is the first alemtuzumab desensitisation reported from our country. We have chosen a 12-step protocol because it is safer and is published and widely accepted. A careful risk/ benefit ratio should be considered for all patients before desensitisation.

Written informed consent was obtained from the patient.

TABLE 1. 12-step, 3 bags desensitisation protocol with Alemtuzumab

	Volume (ml)	Concentration (mg/mL)	Total amount (mg)			
Solution 1	10	0.01	0.1			
Solution 2	10	0.09	0.9			
Solution 3	80	0.137	11			
Step	Solution	Infusion rate (ml/min)	Time (min)	Volume (ml)	Administered dosage (mg)	Cumulative dosage (mg)
1	1	2	15	0.5	0.005	0.05
2	1	5	15	1.25	0.0125	0.0175
3	1	10	15	2.5	0.025	0.0425
4	1	20	15	5.75	0.0575	0.1
5	2	5	15	0.5	0.045	0.45
6	2	10	15	1.25	0.1125	0.5625
7	2	20	15	2.5	0.225	0.7875
8	2	40	15	5.75	0.5175	0.9
9	3	10	15	7.5	1.02	1.02
10	3	20	15	12.5	1.71	2.73
11	3	40	15	20	2.74	5.47
12	3	80	15	40	5.48	11

TP1436 | Successful desensitization in a patient with methimazole induced serum sickness disease

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Case Report:

Background: Methimazole is a drug used to treat hyperthyroidism. Serum sickness disease is a type III hypersensitivity reaction. Few cases of methimazole induced serum sickness have been reported. Diagnosis is made on the basis of knowledge obtained by medical history and physical examination. When the therapeutic alternative is ineffective or does not exist, desensitization (usually recommended for type I reaction) may be a solution for this type of immunological reaction.

Case report: A 36-year-old woman, diagnosed with Basedow-Graves disease was referred to our clinic 1 month after discontinuing her anti-thyroid therapy. She first started treatment with methimazole, but, 2 weeks later, she developed symptoms compatible with serum sickness disease (extensive rash, arthralgia with important articular dysfunction and lymphadenopathy). Laboratory work-up revealed hypocomplementemia. A short course of oral corticosteroid was decided with complete resolution of symptoms. Later on, propylthiouracil was decided as an alternative treatment. After three months of therapy, another significant adverse reaction (toxic hepatitis with AST = 119.62 U/L, ALT = 223.75 U/L, ALP = 110.41 U/L) imposed propylthiouracil discontinuation.

The patient was referred to our tertiary drug allergy clinic for allergy work up and therapeutic decision. At that time, antithyroid treatment was imperious necessary (fT4 level was 20.61 pmol/L (9-19), and TSH level was 0.0004 µIU/mL (0.51-4.3)).

Physical examination revealed diffusely enlarged and smooth thyroid gland, protruding eye with tearing; no other abnormalities were detected.

Atopic status was demonstrated after skin prick tests, with subclinical sensitization to mites and ragweed pollen.

We decided to apply a desensitisation schedule with a pre-treatment regimen with H1 antihistamines and low dose of oral corticosteroid (the latter being also indicated for her endocrinologic condition).

Results: During hospitalization, in a protocol of 6 days desensitisation, our patient progressively received a final safe dose of 15 mg/d methimazole (starting from 2.5 mg/d). At the time of this case report, she remains free of symptoms.

Conclusion: Methimazole-induced serum sickness is a rare condition. To our knowledge, this is the first report of successful drug desensitization to methimazole in a patient with Basedow -Graves disease and with methimazole induced serum sickness disease.

TP1437 | Successful rapid push subcutaneous desensitization in a patient with delayed local hypersensitivity reactions to immunoglobulins

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Case Report:

Background: A 57-year-old man presented with recurrent respiratory tract infections in the context of panhypogammaglobulinaemia. He commenced subcutaneous immunoglobulin (SCIg) with 10 mL administered in the abdomen. He presented the day after the 1st infusion with erythema and pain across his abdomen persisting for 72 hours. Alternative products were infused with pre-treatment of prednisolone, paracetamol and cetirizine but he experienced the

Week	Concentration (mg/mL)	Volume (mL)	Daily dose (mg)	Weekly cumulative dose (mg)
1	200	1	200	1000
2	200	1	200	1000
3	200	1	200	1000
4	200	1	200	1000
5	200	2	400	2000
6	200	2	400	2000
7	200	4	800	4000
8	200	4	800	4000
9	200	8	1600	6400
10	200	8	1600	6400
11	200	10	2000	8000
12	200	10	2000	8000

same reaction. Sequential tryptase levels at baseline and after reactions were normal. Anti-IgA testing was negative. He switched to intravenous immunoglobulin (IVIg) and was pre-treated with IV hydrocortisone, oral paracetamol and cetirizine. He initially tolerated this but after subsequent infusions he developed erythema and pain in the arm persisting for 2 weeks. The same symptoms occurred despite switching products. Subsequently, skin testing, followed by a dose ranging study and desensitization to immunoglobulin, were proposed with informed consent obtained.

Methods and Results: Skin prick and intradermal tests (IDTs) were performed with neat solutions of 4 SCIg and 2 IVIg products. All skin prick tests were negative. IDTs were read at 15, 30 and 60 minutes, 24 and 72 hours and 1 week. IDTs were positive to 2 SCIg products at 24 hours. A dose ranging study for 200 mg/mL SCIg was performed commencing at 1/8000 of the total weekly dose with pre-treatment of cetirizine, prednisolone and omeprazole. He had localized swelling and pain at 24 hours after administration of 400 mg. A skin biopsy was performed that showed a mild perivascular lymphocytic infiltrate and rare mast cells. Direct immunofluorescence was negative. A slow desensitization for 200 mg/mL SCIg was developed (table 1), starting at the last tolerated dose of 200 mg. Given the presence of mast cells, premedication with high dose cetirizine was introduced. The 200 mg dose was tolerated, so he then administered this as daily rapid push, achieving a cumulative weekly dose of 1 g. Daily push dose was escalated when the existing dose was tolerated with only minor local reactions. The patient ultimately self-administered a full weekly dose of 8 g without further problems.

Conclusion: To our knowledge, this is the first report of a successful subcutaneous desensitization in a patient with severe delayed reactions to SCIg and IVIg. The mechanism of the reactions remains elusive but tolerance was achieved by minimal dose increment and antihistamines at high dose.

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DIFFERENT ASPECTS ON DRUG HYPERSENSITIVITY

TP1440 | Sensitization to mepivacaine in a 10 years old patient

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Case Report:

Background: Mepivacaine is a widely used local anesthetic; however, documented hypersensitivity reactions are exceptional, especially in children. Cross-reactions between mepivacaine and other amides appear to be relatively frequent, although there is no defined pattern of reactivity between the drugs in the group. We report a 10 years old non atopic boy who had an urticaria reaction during an endodontics. He was diagnosed of immediate mepivacaine hypersensitivity, confirmed on provocation testing.

Methods: Skin prick test with mepivacaine, lidocaine and latex were performed. Intradermal skin test with mepivacaine and lidocaine in 1/10 dilution and subcutaneous exposure test with pure mepivacaine and lidocaine were also performed.

Results: Skin prick test were negative for mepivacaine, lidocaine and latex. Intradermal test with mepivacaine and lidocaine in 1/10 dilution were also negatives. Subcutaneous exposure test with pure mepivacaine was positive. Subcutaneous exposure test with pure lidocaine was negative.

Conclusions: Mepivacaine is one of the most used local anesthetics, and however, the described cases of hypersensitivity to it are exceptional. We describe a case of a 10 years old patient with no previous history of atopic disease, who present specific sensitization to mepivacaine with good tolerance to lidocaine. The increase in this type of reactions can be expected in the coming years in both children and adults.

TP1441 | Generalized paralysis induced by local lidocaine injection

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Case report: Local anesthetics, such as lidocaine, are widely used for numbing. Adverse drug reactions related to lidocaine are variable, unpredictable, and rarely reproducible, with the exception of some typical cases.

A 42-year-old female who had shown a bizarre neurological reaction after lidocaine injection for dental procedures was referred for diagnosis and safe anesthetic alternatives. Within a few minutes after exposure to lidocaine, she was unable to move any extremity, or to speak, while sensory and high cranial nerve functions were preserved. She was alert and able to communicate with eye blinks. This reaction was repeatedly reproduced after intradermal injection of 2% lidocaine, with complete recovery within 1 h without treatment. No cross-reactivity with mepivacaine and bupivacaine was observed.

This is the first report of immediate and transient generalized paralysis related to lidocaine.

TP1442 | Acute urticaria due to a vasoprotective drug

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Case report: A vasoprotective is a medication which acts to alleviate certain conditions of the blood vessels. Hidrosmin is one of these drugs. It is widely used both in everyday life and in the nursing care. It is usually well tolerated, and there are scarce reports of allergic reactions in our environment

Urticaria is not a frequent adverse effect of vasoprotective drugs.

We report on a 57-year-old male who, immediately after cleaning with chlorhexidine gel and of the application of hidrosmin as preparation for a nursing intervention in left inferior limb developed acute urticaria in this limb, which reverted in approximately five hours with systemic steroids.

She had previously tolerated both products without any problems.

Skin prick-tests with chlorhexidine and hidrosmin were realized in eleven healthy control subjects.

Skin prick-tests with chlorhexidine (10 mg/mL), hidrosmin (0.2 mg/mL) and latex were realized in the patient.

Controlled topical challenge was realized with chlorhexidine in the patient.

The prick-test with chlorhexidine and hidrosmin were negative in eleven healthy control subjects.

Skin prick-tests with chlorhexidine and latex were negative in the patient.

The patient tolerated without incidences the controlled topical challenge with chlorhexidine.

Skin prick-tests with hidrosmin were positive in the patient (8x6 mm): We report on a case of immediate urticaria due to hidrosmin and triggered by an immediate, probably IgE-mediated, hypersensitivity mechanism.

Some of the drug used in daily clinical practice can cause allergic contact urticaria and should therefore be borne in mind.

TP1443 | Allergy to titanium - paradoxes in dentistry

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Background: Allergy to titanium is believed to be quite rare. Well, titanium is widely used in medicine (dentistry, traumatology and orthopedics). However, titanium oxide often used in pharmacy as a component of tablets. Thus, the majority of the population can have a hidden sensitization to titanium.

Purpose: study features of titanium allergy in dentistry.

Method: 3021 patients from Saint-Petersburg dental clinic at the age 18-84 years, 2240 women and 781 men were examined of these during 2014-2018. The patients underwent allergy testing in vivo: patch – tests, confirmed by provocative tests in dental cavity, using original intrabuccal method of diagnosis allergy by increasing peroxidase activity in saliva.

Results: Patch-tests to titanium were positive in 242 cases (8 percent of patients).

Conclusion: 1. Allergy to titanium is not rare.

2. In order to avoid the financial costs, associated with re-prosthetics, it is necessary to pre-test allergy in individuals.

3. Requires the creation of acceptable commercial tests for the diagnosis this type of allergy.

TP1444 | The “red man syndrome” followed by vancomycin-induced leukocytoclastic vasculitis

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Case report: The red man syndrome is the most frequent cutaneous reaction from vancomycin. It is related to the infusion of antibiotics, release of histamine, from mast cells with a mechanism related to immunoglobulin E. Antibiotics such as ciprofloxacin, amphotericin B, rifampicin and teicoplanin can potentially cause red man syndrome. If the antibiotics are mixed with vancomycin and opioid analgesics, muscle relaxants, or contrast dyes the effects are far worse. Vancomycin also has the potential to cause immune-mediated reactions, or hypersensitivity reactions, which may be less frequently recognized. Vancomycin HSRs include immediate, type I; organ specific reactions such as acute interstitial nephritis, typically a Type II; and other non-immediate HSRs, commonly type IV. These HSRs include maculopapular rash, drug rash eosinophilia and systemic symptoms syndrome, linear IgA bullous dermatosis, and Stevens-Johnson syndrome/toxic epidermal necrolysis. However, cases of vancomycin-induced leukocytoclastic vasculitis are rare.

A 57-year-old male with past medical history of hypertension, hyperlipidemia, mitral valve replacement became our patient. The patient was admitted in the infectious department for possible sepsis, suspected MRSA endocarditis, and treated empirically with intravenous ceftriaxone 2 g/ 24 hours, intravenous vancomycin 15 mg/kg body weight every 24 hours.

On the fourth day of treatment, he complained about the typical symptoms of “red man syndrome”. Lab and immunologic exams were almost normal. Vancomycin was interrupted, and the severe condition was treated intensively for 12 days. The patient was readmitted in our clinic with palpable purpura and maculopapular rash appearing first on the lower limbs. The cutaneous manifestations had spread to mid-thigh, abdomen, and chest. While the erythrocyte sedimentation rate was elevated to 45 mm/h, his immunological work-up including c-ANCA, p-ANCA, and atypical ANCA were negative, and C3 level was low.

A severe leukocytoclastic necrotizing small cell vasculitis consistent with hypersensitivity vasculitis related to drug therapy, was revealed after a skin biopsy. Literature shows that the onset of vancomycin-induced LV can be highly variable, ranging from within 24 hours after drug initiation to as late as 1 month after administration. Our patient's case can be considered as a delayed complication of vancomycin therapy as a relapse of red man syndrome on the 20-th day of the starting of vancomycin.

TP1445 | Erythropoietin allergy in a patient on hemodialysis

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Background: Recombinant human erythropoietin is an important therapy for anemia due to chronic renal failure. Allergy to recombinant human erythropoietin is rare and there is only few data regarding the diagnosis of skin tests.

Method: Case presentation: 41-year-old patient with chronic renal failure due to sarcoidosis, with secondary anemia, has been evaluated for suspected erythropoietin allergy. After 5 months of subcutaneous therapy with epoetin zeta (retacrit 400) the patient showed local reaction of erythema and pruritic edema of the drug administration site, 10-15 cm in diameter, a couple of hours after administration of the drug. The regression of the symptoms occurred in the following days, with the use of topical steroids and systemic antihistamines. Epoetin zeta was substituted with darbepoetin alfa (aranesp), but the patient showed the same skin reaction, after the first administration, but more pronounced. The patient did not show any systemic symptoms.

Results: Diagnostic approach: We performed skin tests (prick test and intradermal test) with epoetin zeta and with darbepoetin alfa. The prick test 1/1 resulted positive for derbepoetina ++. Epoetin zeta resulted negative for prick test 1/1, but positive the intradermal test 1/10000 + +.

We noticed that both drugs contained polysorbate - polysorbate 20 as excipient of epoetin zeta, and polysorbate 80 for darbepoetin zeta.

So we performed cutaneous test for polysorbate 20 and 80: prick test 1/1, ID reaction 1/10000, 1/1000, 1/1000 and 1/10, resulted all negative.

We also tested epoetin beta (mircera), containing polietilenglicol, resulted positive for the prick test 1/1 + + .

Conclusion: The data in the literature suggest the preservative (polysorbate with various chain lengths) the most probable cause triggering hypersensitivity. However, given the negativity of skin tests for polysorbate 20 and 80 and for polietilenglicol and the positivity for the 3 tested epoetins, in this case the most probable hypothesis is the allergic sensitization to the erythropoietin; however, the formulation without preservatives is not available. Allergic skin tests may be a simple diagnostic method in the suspicion of an allergy to epoetin.

TP1446 | Dextromethorphan allergy

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Case Report:

Rationale: Dextromethorphan is commonly used, effective, and relatively safe non-opioid antitussive medication. It is available over-the-counter as a single medication (not available in UK) or in combination with other common medications used for flu and cough symptoms' relief. Adverse reactions are infrequently reported and usually are not severe. Symptoms usually are dose-related, these may include mild symptoms such as gastro-intestinal upset, or severe neurological side effects such as dysfunctional speech and ataxia. We report 2 cases of dextromethorphan allergy to therapeutic doses of dextromethorphan in over the counter cough medications.

Case report: First patient was a 49 year old lady presented to Immunology clinic, She was known to have hypersensitivity to NSAIDs but tolerant to paracetamol. She also had a history of anaphylaxis to over the counter cough preparation (Night Nurse). This was not previously explored. She presented with further anaphylaxis to another cough preparation. Further investigations confirmed dextromethorphan was a common ingredient. Macrogol was also present in both preparations; however, investigations confirmed tolerance to macrogol.

Second patient was a 31 year old non atopic patient was referred to Immunology having had anaphylaxis after taking over the counter cough preparation (Covonia). He had further reaction after taking "day and night" night preparation. However, he has tolerated the "day and night" day preparation. Dextromethorphan was thought to be the culprit following review of ingredients of the relevant medications and known tolerance to other potential allergens.

Discussion: Dextromethorphan essentially is a methylated dextrorotatory analogue of levorphanol, which is a phenanthrene derivative. In contrast to other phenanthrene derivatives, such as codeine or morphine, dextromethorphan has no analgesic, or physical dependence–producing properties. This adds to its popularity and widespread use in various age groups. There are only 2 previous reports of anaphylaxis to dextromethorphan.

Conclusion: These two cases illustrate a significant and potentially severe systemic reaction to a commonly used and presumably safe active ingredient in over-the-counter cough and cold preparations. This report highlights the requirement to consider all ingredients of the culprit medications although it may have not been reported directly in the history.

TP1447 | Sialadenitis induced by iodinated contrast: "Iodide mumps"

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Background: Acute swelling of the submandibular, sublingual and parotid salivary glands is an uncommon complication to the administration of iodinated contrast media, which can occur from minutes to five days after exposure. This unusual reaction is also known as "iodide mumps". The course is usually benign and rapid resolution of symptoms is expected without treatment within a few days. The etiology remains unclear, but the reaction seems to be idiosyncratic or related to toxic accumulation of iodide in the ductal systems of the salivary glands. Despite the initial idea, the introduction of non-ionic contrast media has not eliminated the risk of developing iodide mumps.

Method: We report four cases (2 men, 2 women; mean age 64) who suffered episodes of bilateral, painless, cold inflammation of the salivary glands (submandibular and parotid) after the administration of radiological contrast media (CT scan). Initially, the neck swelling in these patients was attributed to an allergic reaction, for this reason they were referred for allergy study. In all cases, the symptoms disappeared spontaneously within 48-72 h. Only one patient had renal failure and related a previous episode of salivary gland swelling after a iodinated contrast administration. As in this case, previous studies have reported that repeated administration of radiological contrast media produce recurrence of iodide induced mumps. An allergological study was performed by skin test (prick and intradermal reaction) with the radiological contrast media involved. In some of the cases, an ultrasound could be performed.

Results: The allergic etiology was ruled out by anamnesis and skin tests. Results of prick and intradermal tests with iodinated contrast media were negative in all cases. Other pathologies were discarded by differential diagnosis. Ultrasound imaging of the glands showed diffuse swelling and prominent internal low-echoic septa, typical findings of iodide mumps.

Conclusion: Salivary gland enlargement following iodine administration is a rare event and only a few cases have been reported. The diagnosis should be suspected when patients present with neck swelling after the procedure. The prompt recognition of this complication should result in the avoidance of an expensive investigation and the expectation of rapid, complete recovery. The efficacy of premedication in order to prevent these reactions is questioned, for this reason it is advisable in these cases to use imaging systems without iodide-based contrast media.

TP1448 | The multiple faces of dimethyl fumarate (tecfidera) drug hypersensitivity

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Case Report:

Background: Dimethyl Fumarate (DMF) is a fumarate derivative -important oral treatment option for various autoimmune diseases, such as psoriasis and multiple sclerosis (MS). It was approved by the European Medicines Agency (EMA) in early 2013 for use in European Union as Tecfidera. As such, DMF is a fine white crystalline powder, which is used extensively in the Asian leather industry to prevent mould growth in finished leather products, such as couches, sofas, shoes. There are reports of delayed-type contact dermatitis and contact urticaria to footwear, clothing and furniture, attributable to DMF. We report a first clinical case of Tecfidera, administered orally for relapsing- remitting multiple sclerosis, drug hypersensitivity reactions.

Case Report: A 43-year-old woman with MS exhibited an acneiform rash affecting the upper trunk about 8 months after starting Tecfidera. Skin biopsy from one of the lesion showed a well circumscribed area of suprabasal acantholysis with associated overlying dyskeratosis, consistent with Grover's disease. The skin eruption faded after stopping Tecfidera. 1 month later patch test with European Baseline Series, (Meth) Acrylate Series (Chemotechnique Diagnostics) and Tecfidera 0.1% in pet was performed. The patch test proved positive to Cobalt (II) chloride hexahydrate and Tecfidera. Oral provocation test with Tecfidera also was positive: flushing, generalized erythema, intense pruritus recorded 1 h after last dose (total dose 480 mg). Diagnosed based on clinical findings, provocations and skin biopsy. Treatment was adjusted to Teriflunomide (Aubagio) and no new symptoms were observed since. The clinical response was good, with no significant adverse effects, we did not prescribe desensitization to DMF.

Conclusion: We report a multiple different adverse events (Grover's disease, Red man syndrome) induced by one medication in the same patient.

TP1449 | Photo-induced telangiectasia: An uncommon dermatological side-effect to many drugs

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Background: Cutaneous adverse drug reactions are the clinical expression of immunological or non-immunological processes, like photosensitivity.

Method: We report our experience on 16 patients, observed between 2015 and 2017, who developed eruptive telangiectasias in photoexposed areas after drug intake. All patients underwent physical examination, laboratory investigations (total blood count, electrolytes, liver function indices, ANA, anti-ENA, anti-La, anti-Ro, ANCA, and anti-Scl-70 antibodies), patch test with standard series of photoallergens and variable concentrations of the drugs used, and provocation test with UVA and UVB. In some cases, we could perform biopsy and histological examination of skin lesions.

Results: Dermatological examination revealed subcentimetric telangiectasias only in sun-exposed areas (face, presternal region, back of the nose, shoulders, arms). Lesions occurred 10-60 days after the beginning of systemic therapies with antibiotics, antidepressants, antihypertensive or anti-inflammatory drugs.

None of the patients had a history of photosensitivity, nor had applied topical drugs on involved areas. Laboratory investigations did not suggest autoimmune or haematological diseases.

Patch tests were negative. Provocation tests with UVA and UVB caused the onset of telangiectasias on irradiated skin after 24-48 hours. Histological examination showed enlarged capillaries in the upper dermis, without signs of vasculitis, and a perivascular lympho-histiocytic infiltrate. Telangiectasias disappeared after drug withdrawal and systemic therapy with corticosteroids. Six months after discontinuation of the drug, provocation test with UVA and UVB did not elicit telangiectasias.

Conclusion: Distribution of lesions and clinical history suggest correlation between onset of telangiectasias, sun exposure (particularly intense in our geographic area) and drug intake. Pathomechanisms are unclear; likely, photoactivation of drugs by UVA and/or visible radiations produces reactive oxygen species and/or photoadducts, leading to vasodilation and endothelial damage. Drug-induced cutaneous telangiectasias are probably often misdiagnosed. Detailed medical history is essential for correct diagnosis. Discontinuation of the responsible drug and therapeutic switch to another pharmacological class are mandatory.

TP1450 | Ondansetron: Friend or foe?

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Case Report:

Background: Ondansetron is a 5-hydroxytryptamine (5-HT_3) receptor antagonist used very frequently as an anti-emetic drug in prevention and treatment of chemotherapy-induced nausea and vomiting but also in the intraoperative environment. There are only a few rare cases described in literature and in addition allergic reactions can be fatal. Allergy to 5-HT_3 receptor agonists has been described as a class effect; however, some authors have suggested that it may be drug specific. Some of these drugs, as ondansetron and tropisetron, share the same heterocycle indol, while granisetron and palonosetron do not and could be alternative drugs to consider.

Clinical Report: A 21-year-old woman referred to our immunoallergology outpatient department for anaphylaxis during intervention for lipoma excision. During the procedure, the patient underwent anesthetic induction with administration of fentanyl, propofol, rocuronium and dexamethasone. Subsequently, on anesthesia recovery was administered neostigmine, atropine (decurarization) and ondansetron. Immediately after decurarization she presented an episode of hypotension (68/32 mmHg), supraventricular tachycardia (160 bpm), diaphoresis, dyspnea and cough with mucous expectoration. After administration of hydrocortisone, clemastine and ranitidine the symptomatology improved progressively after 60 minutes. The patient had a previous history of allergic rhinitis and no history of drug allergy. The authors performed skin prick and intradermal tests with dexamethasone, rocuronium, propofol, atropine, neostigmine and ondansetron according to the concentrations recommended by the ENDA/EAACI drug allergy interest group. All were negative except for immediate intradermal tests with ondansetron at a concentration of 1:100.

Conclusions: The authors describe a severe case of allergy to ondansetron diagnosed by skin tests. The next step in the study of this patient may be the evaluation of sensitization to granisetron or palonosetron, given the structural difference, allowing the administration of a 5-HT_3 receptor agonist in case of need.

TP1451 | Hypersensitivity to antituberculosis drugs in patients with pulmonary tuberculosis

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Background: Objective. Determine the frequency, structure of drug hypersensitivity in patients with pulmonary tuberculosis and its effect on the results of patient treatment.

Method: The case histories of 449 individuals with chemosensitive destructive tuberculosis who received antimycobacterial drugs in 2008-2017. For the diagnosis of hypersensitivity, clinical and anamnestic data, the results of skin and laboratory tests with drugs (isoniazid, rifampicin, pyrazinamide, ethambutol, streptomycin) were used.

Results: Hypersensitivity to drugs was detected in 92 (20.5%) of 449 patients. The mild (itching, acute urticaria, isolated blood eosinophilia) clinical manifestations we attributed 62 (67.4%) of 92 cases. A moderate degree (acute urticaria, angioedema, eczematous dermatitis, multiforme exudative erythema) occurred in 25 (27.2%) of 92 patients with tuberculosis. Severe (anaphylactic shock, Lyell's syndrome, cardiac arrhythmia, nephrotic syndrome) were observed in 5 (9.4%) of 92 patients with hypersensitivity.

The largest share among cause-significant allergens in the development of drug allergy in the subjects studied the following drugs: streptomycin - 23.9%, isoniazid - 17.4%, rifampicin - 13.0%, pyrazinamide - 10.9%, ethambutol - 6, 5% of cases. At the same time, in 15 (16.3%) out of 92 examined with the presence of hypersensitivity more than one drug was identified as cause-significant allergens. In 11 (12.0%) patients, follow-up drugs (vitamin preparations, mucolytics/mucoregulators, analgesics/antipyretics) became the cause of development. Allergy in patients with destructive sensitive tuberculosis slowed down the cessation of bacterial excretion (after 2 months of treatment, sputum negativity was observed in 78.7% of people without allergies versus 60.9% with its presence, $P < 0.05$) and healing of destruction cavities in the lungs (through 3 months of treatment in patients without allergy, cicatrization of destruction was noted in 47.9% of individuals versus 32.6% of those examined with the development of allergy ($P < 0.05$).

Conclusion: Allergy occurs in every fifth patient with chemosensitive destructive TB. Among cause-significant allergens, streptomycin, isoniazid and rifampicin predominate, less often pyrazinamide, ethambutol and maintenance drugs act as allergens. The development adversely affects the efficiency of treatment of patients with TB, significantly reducing the frequency of termination of bacteria excretion and elimination of pulmonary parenchyma.

TP1452 | First line antituberculosis drug hypersensitivity: Culprit two drugs

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Case Report:

Background: Pulmonary tuberculosis is treated with multiple drugs. Drug allergy with medications used in treatment may be complicated. Here we report the case of allergic reaction to 2 antituberculosis drugs.

Case: A woman, forty six years old, patient was diagnosed culture positive pulmonary tuberculosis and treated with isoniazid,

rifampicin, ethambutol and pyrazinamide. The treatment was discontinued on the 13th day due to the development skin erythematous lesions compatible with urticaria. The clinical situation taken under with anti-histaminics and all anti-tuberculous drugs were stopped. Allergy tests were performed for the suspected drugs with graded challenge. Reaction (urticaria and erythema) with rifampicin and pyrazinamide was observed. The reaction improved with antihistamines and methylprednisolone. There was no reaction with ethambutol and isoniazid. The patient was consulted with tuberculosis clinic. The treatment was changed to isoniazid, ethambutol, streptomycin and moxifloxacin. These drugs were given with the graded challenge. No reaction was observed with these drugs. The patient is on treatment with these drugs without any event for the last three months.

Conclusion: Pulmonary tuberculosis is treated with multiple drugs. At this time, drug allergy may be related to one or more drugs. In this patient we observed allergy with rifampicin and pyrazinamide. The new treatment regimen was administered. It was also possible drug desensitization in case of limited alternative treatment.

TP1453 | A rare case of drug allergy; multi-drug resistant tuberculosis

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Case report: Introduction: Multidrug resistant tuberculosis (MDR-TB) is a resistance to both isoniazid and rifampicin, and resistance to other drugs may develop. Multidrug resistant tuberculosis treatment is performed only by experienced specialists in special centers and hypersensitivity reactions may occur during treatment. Case: A 27-year-old female Chechnya patient applied to the same clinic as her brother, who is undergoing MDR-TB treatment, with complaints of cough, weight loss and sputum. Miliary tuberculosis was diagnosed. In bronchoalveolar lavage, TBC-PCR positive, INH + RIF resistance was determined. Moxifloxacin 400 mg, Ethionamide 750 mg, cycloserine 750 mg, Pyrazinamide 2000 mg, Ethambutol 1500 mg, PAS 9 g, methylprednisolone were initiated. The patient was also followed up due to diffuse choroiditis and suspicion of tuberculosis meningitis. On the 28th day of the treatment, it was discontinued due to widespread itching and rash on the body. She was referred to us after 9 days. No active skin lesions were detected. Since the general condition of the patient was worsening and diffuse systemic, moxifloxacin 400 mg and amikacin 1 gr were divided into 4 doses and started with 1 hour interval. One day apart and respectively; ethambutol 1500 mg desensitization, cycloserine 750 mg oral provocation were performed. In her follow up, changes in consciousness, involuntary contractions in the extremities, cycloserine was removed from the regimen. Next, linezolid 600 mg, protionamide 750 mg, PAS 8 gr was given oral provocation. Treatment with moxifloxacin, amikacin, EMB, Linezolid, Thonamide, PAS, methylprednisolone was continued.

Conclusion: MDR-TB treatment is an excessive and long-term treatment regimen with side effects and drug reactions. Treatment is mandatory and in this case, successful desensitization was performed after drug reactions during MDR-TB treatment.

TP1455 | Vaccine-induced hypersensitivity: What's the value of skin tests ?

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Background: The usefulness of skin tests in the diagnosis of vaccine hypersensitivity (VH) has been rarely assessed previously. Aim: To analyze the clinical and chronological features of vaccines-induced hypersensitivity notifications and to evaluate the value of skin tests in the diagnosis of the VH.

Method: We carried a descriptive study (2004-2018) including all cases of suspected vaccine-induced hypersensitivity and notified to the Pharmacovigilance Department of Monastir (Tunisia). The vaccine imputability was established according to Begaud's method. Skin tests were performed according to ENDA recommendations (*European Network of Drug Allergy*).

Results: We listed 14 notifications of suspected vaccine-induced hypersensitivity (9 men/5 women), with a mean age of 10 years. The average time between the vaccine administration and the onset of VH was 2 days (ranges: 2 minutes to 22 days). Clinical manifestations consisted of a generalized skin eruption in 9/14 patients, which was associated with a facial oedema in 6/14 cases. Based on chronological and semiological considerations, vaccine was thought to be implicated in the hypersensitivity manifestations in 8/14, and the responsibility of this compound was excluded in 3/14. Skin tests (Prick and/or IDT) were performed in 8/14 cases and were positive in 6 of them. The culprit vaccine was the tetanus toxoid (n = 3) and vaccine against Diphtheria (n = 1); however, we did not could discriminate between the responsibility of the three components of combined vaccine DTP (diphtheria-Tetanus-Pertussis) in two other patients. In the remaining cases, three patients were lost to follow-up.

Conclusion: Through the present study, we added to the medical literature a case series of vaccine induced hypersensitivity and we demonstrate the usefulness of skin tests in the diagnosis of VH and in the identification of the culprit vaccine.

TP1456 | Allergic reaction to yellow fever vaccine in a patient with bird-egg syndrome

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Case report: Allergic reactions to yellow fever vaccine have been described in patients with egg allergy. Yellow fever vaccines are

derived from chicken embryo and typically contain chicken egg proteins. Allergy to chicken egg comprises patients with primary sensitization, usually pediatric patients, as well as patients with primary sensitization to birds followed by secondary sensitization to serum albumins present in poultry meat and egg (bird-egg syndrome), observed primarily in adult patients. Here, we present an unusual case with a local allergic reaction to yellow fever vaccine as the first manifestation of a bird-egg syndrome.

A 20 year-old female canary bird keeper developed pronounced erythema, swelling and pruritus of the entire arm few minutes after an injection of yellow fever vaccine in the upper arm. A detailed history revealed that the patient had been suffering from nasal obstruction for years. Previous skin prick testing had failed to demonstrate sensitization to pet dander; however, canary feathers had not been tested. The patient also reported that she tolerates ingestion of egg well, but for personal reasons avoids eating chicken meat. Our diagnostic work-up by means of skin prick testing showed specific sensitization to poultry meat, chicken egg yolk and white, feather mix and feathers of the patient's own canary. Furthermore, laboratory analyses demonstrated increased total IgE (401 IU/ml) and specific IgE to poultry meat, chicken egg yolk and white as well as canary feathers, but not to ovalbumin (Gal d 2) and ovomucoid (Gal d 1).

Based on these results, we diagnosed a bird-egg syndrome, most likely being responsible for the allergic reaction to yellow fever vaccine. Sensitization may have been elicited by serum albumin (Gal d 5) present on feathers of the canaries. Serum albumin is also present in chicken meat and egg yolk, but not egg white, whereas the cross-reacting ovalbumin constitutes the main protein of egg white, thus matching the diagnostic findings in our patient. Tolerance to egg in our patient can probably be explained by the heat instability of serum albumin. To our knowledge, allergic reactions to vaccines have so far not been reported in patients with bird-egg syndrome.

TP1457 | Paclitaxel induced pemphigus vulgaris in a patient with ballon angioplasty

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Case Report:

Background: Pemphigus vulgaris is an autoimmune disease characterized by the presence of flaccid blisters of the skin and/or mucosae. "Drug-induced pemphigus" is defined by the presence of pemphigus lesions induced by systemic ingestion or local use of drugs. Paclitaxel drug coated balloon (PDCB), recently introduced in interventional cardiology, delivers the antiproliferative drug to the local arterial tissue by single, prolonged inflation of the coated balloon thus preventing restenosis and leaving no implant behind. Skin adverse effects of paclitaxel are frequent, mostly through toxic or non-immunological mechanism, but no case report of paclitaxel induced pemphigus has been reported.

Material and methods: We present the case of a 66 years old man who developed flaccid blisters on the skin of the scalp and upper trunk and erosions on the oral mucosa. 3 weeks before the beginning of this episode he has had a percutaneous coronary intervention with PDCB for the treatment of a severe occlusion of the second diagonal artery. The clinical exam revealed lesions compatible with the diagnosis of pemphigus vulgaris, that was confirmed by histopathological exam. Direct immunofluorescence staining revealed IgG antibodies on the intercellular and transmembrane domains of keratinocytes within the epidermis. The patient was started on oral prednisone 25 mg daily, but new lesions continued to appear. We also decreased the number of drugs used. He continued only on Clopidogrel, Verapamil and Metoprolol. After one month of Prednisone 25 mg daily the dose of oral corticosteroid was increased to 60 mg daily, with no clinical benefit. A new treatment was started with Methylprednisolone and Azathioprine. The latter was discontinued because of adverse drug reactions (nausea, malaise). The clinical course was slowly favorable, without any new blisters and the dose of Methylprednisolone was tappered to 16 mg daily. At the time of this report, the patient is stable, without new blisters.

Discussion: Although we do not have criteria or biomarkers for defining drug - induced pemphigus, the history in this patient can be compatible with paclitaxel induced pemphigus. The time period between the coronary intervention with PDCB and the development of the first symptoms was three weeks, and the clinical response to systemic corticosteroids is consistent with the half life of paclitaxel delivered through drug coated balloon.

TP1458 | Gentamicin allergy – a case report

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Case report: Aminoglycosides are an important antibiotic group with generally low resistance and good effect in Gram-negative infections. Nephrotoxicity and ototoxicity are well known adverse effects. Drug hypersensitivity reactions in the form of contact dermatitis are frequent due to sensitisation following topical treatment with neomycin. Other examples of cutaneous manifestations include urticaria, maculopapular exanthem and fixed drug eruption. Serious reactions such as DRESS or toxic epidermal necrolysis are rare. There are only sporadic case reports of IgE-mediated reactions or anaphylaxis to aminoglycosides. Asymptomatic sensitisation to neomycin in children is common (11.5%).

Seven-year-old girl with a background history of vesicoureteral reflux and frequent urinary tract infections requiring various antibiotics in the past and a long-term prophylactic treatment was admitted

with an acute pyelonephritis. She was treated with a combination of amoxicillin/clavulanic acid and gentamicin based on urine culture results. Generalized urticaria with angioedema appeared on the third day of hospital admission during a gentamicin infusion followed by nausea and drowsiness. Clinical diagnosis of gentamicin allergy was later confirmed by skin testing with an immediate reaction to gentamicin in an intradermal test. A drug challenge test confirmed amoxicillin/clavulanic acid tolerance.

We describe a rare case of an IgE-mediated allergy to gentamicin in a paediatric patient.

TUESDAY, 4 JUNE 2019
TPS 48
ANGIOEDEMA AND MASTOCYTOSIS

TP1459 | The need for individually tailored prophylaxis with C1-INH concentrate in pediatric patients with hereditary angioedema (HAE) – real life data

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Background: Hereditary angioedema due to C1-inhibitor deficiency (HAE-C1-INH) is a rare autosomal dominant inherited disease. The recurrent swelling attacks such as subcutaneous edema and colic-like abdominal pain negatively affect quality of life (QoL). Laryngeal edema is rare, but life-threatening if untreated. C1-INH is currently approved for prophylaxis to routinely prevent attacks in patients aged ≥ 6 (EU) and ≥ 12 years (US). Real life data in nine pediatric patients with HAE who received C1-INH concentrate for the routine prevention of angioedema attacks was documented and followed up.
Method: After giving informed consent, the following data were collected and analyzed from patient's diaries and records 1 year before onset of and after introduction of prophylactic treatment: age at first manifestation and diagnosis, age at first treatment, frequency and location of attacks, prophylactic respectively on-demand therapy regimen. Initial standard prophylactic treatment (SP) consisted of 1000 U C1-INH, (bw > 40 kg) or 500 U C1-INH (bw < 40 kg) every 3-4 days i.v. and was intensified (individualized prophylaxis - IP) in case of >2 breakthrough attacks per month. In 2 patients the prophylactic regimen had to be intensified to every 2 days regimen.
Results: Nine patients (4 male/5 female) aged 4.5-17.2 years with HAE-C1-INH type I were enrolled. Attacks before onset of prophylaxis occurred 3-11 times/month and affected mainly abdomen and extremities but also face; a history of laryngeal attacks was reported in six patients. SP resulted in zero break-through attacks in 7/9 patients during a prophylaxis period of 6-41 months. Two patients still presented >2 break-through attacks/month. Consecutive IP resulted in zero break-through attacks in these patients as well during 20-38 months.
Conclusion: These real life data strongly indicate that prophylaxis regimes should be tailored according to the individual patient's needs in order to achieve favorable results.

TP1460 | Long-term prophylaxis with RC1inh in pregnancy in HAE-NC1 INH inh patient

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Background: The management of pregnancy in HAE patients is often a clinical challenge mostly due to the worsening of the disease as a result of the estrogens increase during pregnancy and the lack of standardized treatment protocols. The challenge is even greater when HAE-nC1 INH is the case. There is no evidence to support that mechanical trauma involved in vaginal childbirth could trigger angioedema.
Method: We present a case of a female patient, aged 35, with a positive family history of HAE and diagnosed HAE-nC1 INH with a mutation in the plasminogen gene by next generation sequencing that consorted with disease activity, so we diagnosed her as a fourth type of HAE with normal C1INH levels HAE-PLG.
The patient had several miscarriages in the past 7 years, and during the last pregnancy long-term prophylaxis was discussed as a possible approach. During prophylaxis with tranexamic acid, the patient had developed severe abdominal pain and pronounced fatigue, as well as vision problems, thus it had to be stopped 6 months before the last pregnancy occurrence. At the time, the only available medication was rC1inh, so it was the only option for treatment. Informed consent was obtained and after the first trimester patient regularly received twice a week iv 50 IU/kg bw of rC1inh until the beginning of the last trimester, resulting in reduction of attacks frequency by 83.7% as compared to baseline.
Results: As soon as entering the 38th gestational week, the patient went into labor, less than 2 hours after receiving the last iv dose of rC1inh. The patient had an attack free spontaneous delivery of a baby boy, APGAR score 10, birth weight 3400 gr, length 50 cm. One month after giving birth, patient had no acute HAE attacks and both the baby and mother are doing well. Only rarely do vaginal deliveries cause an edematous attack, with 6% of women not receiving prophylactic treatment according to the PREHAEAT (Novel methods for predicting preventing and treating attacks in patients with hereditary angioedema) study. Those attacks appear immediately after or in the first 48 hours after delivery. Spontaneous vaginal delivery occurs in 80%–90% of births.
Conclusion: In conclusion, rare cases often require individualized treatment and off label use of medications. Clinical practice has shown that off label use of standardized medications can potentially later on become a part of a standardized therapeutic approach in HAE patients.

TP1461 | Hereditary angioedema due to C1-INH: Case report

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Case Report:

Background: Hereditary angioedema (HAE) is a rare disease associated with deficiency in C1 inhibitor (C1-INH), a serum protease inhibitor involved in regulating the activity of multiple proteases. The total/functional deficiency manifests with episodes of cutaneous and submucosal angioedema due to enhanced activation of the plasma contact system and generation of bradykinin.

Case report: A 40-year old man was admitted in Otorhinolaryngology Emergency Department with a 4-hours history of palpebral, lips and tongue edema, dyspnea, throat tightness, difficulty on swallowing. He had no history of drug intake, food allergy, trauma or insects bite. No abnormal signs were observed during systemic examination. Blood tests, chest X ray and abdominal ultrasound resulted normal. Indirect laryngoscopy showed laryngeal edema. He was admitted to the intensive care unit and was treated for anaphylactic reaction with 0.5 ml of (1;1000) 1 mg/ml epinephrine subcutaneous (s.c), prednisolone 100 mg intravenous and oral bilastine 20 mg but no improvement was observed. Emergency tracheostomy was performed. He had experienced several episodes of abdominal pain in his childhood and life-threatening laryngeal attack in 2003 and 2010. In both cases tracheostomy was performed. After the allergologist consult, in view of the patient's actual situation, and a history of repeated episodes of edema the possibility of hereditary angioedema was suspected. Laboratory testing showed a reduced level of C1-INH (0.81 mg/dl). We diagnosed the patient with HAE type I and immediately icatibant (bradykinin B2 receptor antagonist) 30 mg (10 mg/ml) 3 ml s.c was administered. The patient's situation progressed favorably after treatment and he was discharged on the 6th day. Icatibant 30 mg (10 mg/ml) 3 ml s.c was prescribed as short or long-term prophylaxis. He and his family member were informed and educated regarding the disease, its prognosis, trigger factors and the possibility of inheritance. Both his children had low seric levels of C1 esterase even though only the 11-year old girl had experienced occasional abdominal pain episodes.

Conclusion: The diagnosis of HAE is delayed on average by almost a decade due to misunderstanding of symptoms and lack of awareness of the disease. This case emphasizes the role of an early and appropriate diagnosis on improving management and better outcomes.

TP1462 | Hereditary angioedema: 24 cases

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Background: Hereditary angioedema (HAE) is a rare autosomal disorder resulting from deficiency (type I) or dysfunction (type II) of C1 esterase inhibitor (C1INH). It is characterized by recurrent episodes of angioedema without urticaria, affecting the skin or mucosal tissues of the upper respiratory and gastrointestinal tracts. In the last decade, new therapies have been developed for treating or preventing attacks. Nevertheless, HAE is still a barely known disease exposing patients with laryngeal attacks to the risk of asphyxiation. The aim of this study is to evaluate in our service, the clinical characteristics of patients diagnosed with HAE.

Method: 24 patients attending the angioedema outpatient clinic at Gregorio Marañon Hospital were analyzed. HAE diagnosis was established by clinical symptoms and quantitative and/or functional C1-INH deficiency.

Results: Twenty-four patients (55%F, 45%M), average ages of 48.2 y (range: 0-86 y) were included. Family history of HAE was reported in 83.3% of the cases, of these, 20/20 had family members who died of asphyxiation; 62.5% patients became symptomatic before they turned 18 years (median age of 3). The median time between onset of symptoms and diagnosis was 12.5 years. The most frequent triggering factors for attacks were stress (66.6%) and trauma (50%). Prodromes, up to 24 h before the attacks, were mentioned by 8/24 (33.3%) patients: these were erythema marginatum (n = 5), and asthenia (n = 3). During first attack, 17/24 (70.8%) reported peripheral attacks, 4/24 (16.6%) abdominal symptoms, and 1/24 (4.16%) a laryngeal attack. 9/24 patients (37.5%) suffered obstruction of the upper airways in the last year. Three patients remain asymptomatic, of these, one is under two years old and the other 2 are siblings, both in their thirties.

Conclusion: Hereditary angioedema (HAE) is a challenging rare disease, with attacks difficult to differentiate from other angioedema subtypes. In this series, HAE involves a median diagnostic delay of 12.5 years, even though the 83.3% of our patients have family members affected. The awareness of clinical characteristics of HAE among medical staff is essential for an earlier diagnosis and a better management, avoiding complications and improving the quality of life of HAE patients.

TP1463 | Efficacy and safety outcomes for switching to lanadelumab from prior LTP: Findings from an interim analysis of the HELP OLE study

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Background: Patients with hereditary angioedema (HAE) often use long-term prophylaxis (LTP) to prevent attacks. In the EU, lanadelumab was recently approved for routine prevention of recurrent attacks in patients ≥ 12 yrs old. The ongoing HELP open-label extension study, which evaluates the long-term safety and efficacy of lanadelumab, includes patients who did not take part in the prior HELP double-blind study ("non-rollovers") and were using other forms of LTP at the time of enrolment. These patients were permitted to taper off prior LTP early during the lanadelumab treatment period (tapering stage), after which they used lanadelumab only. In this post-hoc analysis of data collected between 26 May 2016–1 Sep 2017, attack rates were compared in patients who tapered vs those who did not taper (ie stopped prior LTP at study enrolment), and during the tapering vs non-tapering stages.

Method: Patients with HAE type I/II received lanadelumab 300 mg q2w during the treatment period, starting on Day 0. Patients who used C1-INH for LTP at the time of enrolment may have continued C1-INH use up to 2 weeks into the treatment period, and those who used oral therapy (androgens/antifibrinolytic) may have continued use for up to 3 weeks.

Results: Data from 63 non-rollover patients who used LTP prior to the first lanadelumab dose were analysed. The change in attack rate (attacks/month) and % change in attack rate from baseline for patients who tapered off LTP vs those who did not taper were similar and were also comparable between the tapering stage and the non-tapering stage (Table). The most common TEAEs for all groups and during the tapering and non-tapering stage were injection site reactions, which is consistent with TEAEs during the overall treatment period.

Conclusion: Attack rate reductions and safety profiles were similar during the tapering stage between patients who tapered off LTP and those who did not taper. Similar results were found in comparing these groups during the non-tapering stage. This suggests a tapering period may not impact the efficacy and safety outcomes of patients who switch to landelumab from prior LTP.

TP1464 | Angioedema's clinical presentation and approach on an emergency department

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Background: Angioedema (AE) is an acute clinical condition and a frequent cause of Emergency Department (ED) visit. A correct approach is essential. However, clinical predictors useful for its diagnosis and treatment are scarce. To assess the clinical presentation, treatment and classification of all patients admitted to Beatriz Ângelo Hospital's ED with diagnosis of AE, since it's opening. We

TABLE. Change in attack rates from baseline.

	Tapering stage* change in attack rate	Tapering stage* % change in attack rate	Non-Tapering stage* change in attack rate	Non-Tapering stage* % change in attack rate
Taper off C1-INH (n = 24)**				
Median (range)	−1.1 (−15.4 to 2.8)	−100 (−100 to 729.1)	−1.0 (−15.0 to 2.7)	−94.6 (−100 to 877.1)
Mean (SD)	−1.7 (3.47)	−33.7 (189.08)	−2.0 (3.22)	−38.4 (211.14)
Taper off oral therapy (n = 7)				
Median (range)	−0.6 (−2.5 to 0)	−100 (−100 to −5.0)	−1.5 (−2.5 to 0)	−100 (−100 to −47.9)
Mean (SD)	−1.0 (0.96)	−84.2 (38.78)	−1.2 (0.95)	−91.3 (21.28)
Did not taper (n = 30)				
Median (range)	−1.8 (−11.1 to 0.5)	−100 (−100 to 30.3)	−2.0 (−10.8 to 0)	−100 (−100 to −17.1)
Mean (SD)	−2.6 (2.49)	−89.3 (28.36)	−2.8 (2.47)	−92.8 (15.77)
No LTP Use (n = 40)				
Median (range)	–	–	−1.5 (−15.0 to 2.7)	−100 (−100 to −14.4)
Mean (SD)			−2.3 (2.58)	−80.5 (99.41)

Data for n = 2 patients who tapered off oral therapy + C1-INH are not included due to small sample size. *The tapering stage was the interval from Day 0 to the day of the last LTP dose, or Day 0-14 for patients who did not taper (in order to compare to the patients who did taper). The non-tapering stage was the interval from the end of the tapering stage to the end of the treatment period. **Results include data from 1 patient who had a high increase in attack rate.

also tried to compare the histaminergic angioedema (hAE) and non-histaminergic angioedema (nhAE) groups.

Method: Retrospective analysis of patients diagnosed with angioedema, laryngeal edema, eyelid edema, pharyngeal/nasopharyngeal edema and periorbital edema from January 2012 to December 2017.

Results: A total of 490 patients was evaluated, 250 with a clinical history suggestive of AE. AE was classified as idiopathic histaminergic (13.2%), idiopathic nonhistaminergic (23.2%), allergic histaminergic (29.2%), related to angiotensin-converting enzyme inhibitors (18.8%), hereditary angioedema with C1-inhibitor deficiency (0.8%) and nonclassifiable (14.8%) according to the 2014 international guidelines by Cicardi et al. They were further divided into hAE (45.2%) and nhAE (54.8%). Forty five percent was considered very urgent. The median age was 45 years (2 to 103), 62.4% were female. In the hAE group 65% of patients were female, 70% were under 18 years old and 21% had rhinosinusitis. Concerning patients with nhAE (59.9% were female) around 89% were older than 18 years old, 9.5% had rhinosinusitis and represented 71% of individuals evaluated by ENT and/or Immunoallergology specialists. Symptoms and location were similar in both groups (eyelids and lips most affected) except for the tongue of which 72.6% were nhAE.

Conclusion: The clinical presentation, age, location and comorbidities seem to differ between hAE and nhAE. These clinical features might be useful on the diagnostic and therapeutic approach of these patients.

TP1465 | An algorithm for diagnosis of hereditary angioedema with normal C1-inhibitor: Applying molecular approach to clinical practice

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Background: Diagnosis of hereditary angioedema with normal C1-inhibitor (HAE-nC1-INH) is often a challenge to the clinician. Mutations in exon 9 of *F12*, the gene encoding coagulation Factor XII (FXII), have been described among patients with HAE-nC1-INH. Recently, mutations in the genes coding for Plasminogen (*PLG*) and Angiopoietin-1 (*ANGPT1*) were also identified in families with HAE-nC1-INH. We investigated the role of allelic discrimination as a tool for diagnosis of patients with FXII-HAE caused by mutation c.983C>A, the most common variant identified in this disease, and proposed an algorithm for diagnosis of patients with HAE-nC1-INH.

Method: 184 individuals including 51 index patients with clinical suspicion of HAE-nC1-INH and their relatives were previously investigated by Sanger sequencing. Allelic discrimination was carried out by real time PCR using probes VIC(554 λmax/nm) and FAM(518 λmax/nm) for wild type allele and the allele with the c.983C>A mutation, respectively. Execution time and costs were compared using Brazilian guidelines. Index patients negative for *F12* mutations were genotyped by Sanger sequencing for mutations c.988A>G and c.807G>T in *PLG* and *ANGPT1*, previously associated with HAE-nC1-INH.

Results: The c.983C>A mutation was found in 96 individuals (24 index patients and 72 family members). 88 individuals were negative for the c.983C>A mutation. Results were 100% concordant by Kappa analysis within the two methods. 71/96 patients positive for c.983C>A mutation were female; 78.9% and 56% were symptomatic female and male patients, respectively. Allelic discrimination presented a 79.8% lower cost and 82.3% less execution time as compared to Sanger sequencing. Mutations c.988A>G and c.807G>T in *PLG* and *ANGPT1* were not found. Among patients negative for *F12* mutations, 11 were diagnosed as Unknown HAE(U-HAE) and 16 as idiopathic non-histaminergic acquired angioedema(InH-AAE).

Conclusion: In areas where the c.983C>A mutation in *F12* is predominant among patients with FXII-HAE, allelic discrimination may be an adequate initial screening method in patients with clinical suspicion of HAE-nC1-INH. Patients with negative results would undergo sequencing of exon 9 of *F12* by Sanger method. Remaining negative patients would be genotyped for previously described *PLG* and *ANGPT1* mutations. Further studies in other areas need to be conducted to establish whether allelic discrimination would have a lower cost and provide faster results.

TP1466 | Burden of hereditary angioedema: Findings from a multinational patient survey in EU, Canada, and Australia

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Background: Hereditary angioedema (HAE) is a rare genetic disorder affecting approximately 1:50 000 people which is characterized by painful swelling attacks of the skin or mucous membranes. The humanistic and economic burden of HAE is thought to be substantial but is not well characterized.

Method: This was a non-interventional, cross-sectional, web-based survey of patients in Australia, Austria, Canada, France, Germany, Spain, Switzerland and the UK with a self-reported physician diagnosis of HAE. Participants were identified and recruited by the member organizations of HAEi (international umbrella organization for the world's HAE patient groups) from July through October 2018 in each of the study countries. Patients with HAE type I/II were eligible if they were ≥ 18 years old, with ≥ 1 HAE attack or prodromal symptom within the last year, received HAE medication within the last two years, and had adequate fluency in the target language for the country in which they resided. Health-related quality of life (HRQoL) was measured using the

AE-QoL and SF-12 questionnaires. The Angioedema Control Test (AECT), Hospital Anxiety and Depression Scales (HADS) and Work Productivity and Activity Impairment (WPAI) questionnaires were administered.

Results: Of the 617 patients screened, 242 (39.2%) met all inclusion criteria and completed the survey. Mean (SD) age was 43.8 (14.7) years, 67.4% of respondents were female and 62.4% currently receive long-term prophylactic treatment. Mean (SD) number of attacks was 12.5 (14.1) during the past 6 mo. and 79.7% reported an attack during the past mo. Prophylactic HAE treatments used in the past year included C1 INH (29.3%), androgens (22.7%), and tranexamic acid (11.2%). Mean (SD) AE-QoL total score was 47.1 (20.7), scores increased (lower QoL) for responders reporting higher attack frequency. Mean (SD) SF-12 mental and physical composite scores were 43.1 (11.2) and 49.3 (9.3). Mean (SD) AECT (disease control) scores were 6.97 (2.97), scores decreased (less disease control) as the frequency of attacks increased. Of 242 respondents, 38.0% and 17.4% reported moderate to severe anxiety and depression on the HADS, respectively. Mean (SD) percentage impairment measured by WPAI was 24.2% (30.0) for work-productivity loss and 33.9% (31.2) for activity impairment.

Conclusion: In this study, patients with HAE had decreased QOL and a high frequency of attacks. Similar results were observed in the US patient survey.

TP1467 | Epidemiological study for type I/II hereditary angioedema disease through a novel dry blood spot (DBS)-based methodology

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Background: Hereditary angioedema (HAE) is an autosomal dominant disease most commonly due to mutations in the *SERPING1* gene, leading to a deficient (type I) or dysfunctional (type II) C1-inhibitor protein which results in excessive production of bradykinin by plasma kallikrein. Clinical manifestations include swelling of extremities, face, upper airways, genitals, and gastrointestinal tract. Abdominal symptoms occur in most patients with HAE and may be the only manifestation of the disease. In individuals with gastrointestinal symptoms, diagnosis of HAE is rarely considered early in the patient journey and can result in misdiagnosis and diagnostic delays averaging up to 8 years. The aim of the study is to investigate the prevalence of HAE in subjects with episodes of unexplained abdominal pain through a novel and simple methodology based on Dried Blood Spot (DBS) collection at point of care and analysis at a central laboratory. Up to 5000 patients with unclear, repetitive abdominal pain attacks referred to Centers other than those specialized in HAE (e.g., Emergency Units) will be enrolled in various countries.

Method: Diagnosis of HAE in this study is based on DBS filter card technology that simplifies sample collection and management. The diagnostic workflow is based on quantification of complement proteins by tandem mass spectrometry (MS/MS) followed by confirmation with genetic analysis. The MS/MS-based quantification of the complement proteins is performed *in situ* by quantifying unique complement peptides for each protein using LC/MRM–MS (liquid chromatography multiple reaction monitoring mass spectrometry). This targeted proteomics approach also distinguishes between HAE type I and II by quantifying levels of C1-inhibitor protein. The biochemical results are genetically confirmed *via* Next-Generation Sequencing of *SERPING1* gene and, when necessary, by MLPA (Multiplex ligation-dependent probe amplification). Enrollment of patients for the Study is ongoing at multiple participating sites.

Results: We expect this study to confirm the capacity of the DBS-based test to identify undiagnosed patients with HAE among individuals with recurrent episodes of unexplained abdominal symptoms.

Conclusion: Results may provide additional epidemiological data in this population of undiagnosed subjects, contribute to increased knowledge of HAE, and facilitate access to instruments to reduce time to HAE diagnosis.

TP1468 | Determinant factors of disease activity in hereditary angioedema due to C1 inhibitor deficiency

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Background: Disease activity is an important feature in hereditary angioedema due to C1inhibitor deficiency (HAE-C1INH) and can decrease health related quality of life (HRQoL). Our objective was to identify determinant factors of disease activity in HAE-C1-INH.

Method: Prospective and observational study. Patients with HAE-C1-INH types I and II ≥ 18 y were included. Demographic, clinical and laboratory data were obtained. HRQoL was measured by HAE-QoL, AE-QoL and EQ-5D-L5 questionnaires and disease activity by Hereditary Angioedema Activity Score (HAE-AS).

Results: Eighty-eight patients were included (44.61 ± 14.9 y, 55.7% women). Mean age at diagnosis was 22.78 ± 15.72 y. and mean in diagnosis delay 15.79 ± 34.10 y. Mean number of attacks within the last 6 months was 6.12 ± 6.69. Women were found to have worse HRQoL than men [AE-QoL (39.43 ± 22.49vs25.60 ± 20.07, $P = 0.04$) and EQ-5D-5L (0.82 ± 0.20vs0.91 ± 0.9, $P = 0.01$)]. Mean score with HAE-AS was 10.16 ± 3.49(1.00-15.62). No correlation of age at diagnosis and actual age was found with disease activity. C4 levels (mg/dl) at diagnosis were lower in patients who had suffered angioedema attacks (7.28 ± 4.02) in comparison to those who had not suffered attacks (9.73 ± 4.54, $P < 0.05$). However, no correlation was found

between complement levels and age, clinical activity or maintenance treatment.

Conclusion: We only found C4 levels at diagnosis as key factors for disease activity.

TP1469 | Mutational spectrum of the SERPING1 gene in a population from southern spanish with hereditary angioedema due to C1 inhibitor deficiency

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Background: Hereditary angioedema due to C1 inhibitor deficiency (C1-INH-HAE) is a rare disorder with a great genetic complexity. More than 400 mutations related to its pathogenesis have been published. We analyzed the mutational spectrum of the SERPING1 gene in our adult population with C1-INH-HAE.

Method: We prospectively studied 116 patients from 37 unrelated families with laboratory and/ or clinical diagnosis of C1-INH-HAE. Our population contains the same proportion of male as female patients(50% male, 50% female). DNA samples were collected from peripheral and all eight exons and adjacent intronic regions of SERPING1 gene were sequenced following standard protocols.

Results: A total of 35 different mutations were identified. We observed a great variability, the mutations comprised 9 frameshift mutations, 4 nonsense mutations, 15 missense mutations, 2 large selection, 1 large insertion, and 4 mutation affecting the splicing sites. Only one large insertion of SERPING 1 gene was detected. We detect mutation in the intron region in one of our families and two families with polymorphisms. Some of the mutations are not published previously.

Conclusion: In our adult C1-INH-HAE population we corroborate the great allelic heterogeneity with each family carrying their own mutation.

TP1471 | Effectiveness of long-term use of danazol in hereditary angioedema: 10 years follow-up at single service in brazil

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Background: Hereditary angioedema (HAE) is a painful and unpredictable disease. The challenge becomes even greater when we deal with the lack of knowledge about the disease and therefore the lack of adequate treatments. Attenuated androgens are the most widely available treatment in the prevention of HAE attacks in our midst. The purpose of this study is to describe the effectiveness and side effects of the long-term treatment with attenuated androgens in patients diagnosed with HAE.

Method: An observational cohort study was conducted with patients diagnosed with HAE and monitored at HC-UFMG. They were evaluated clinically and in laboratory and then submitted to a standardized questionnaire. The collection of data was assembled into a database and a descriptive analysis of it was performed. Variables such as frequency and severity of symptoms before and after danazol, side effects associated with its use and the acceptance of the medication by the patients were studied.

Results: 61 patients diagnosed with HAE were evaluated. From these patients, 45 (73.8%) made continuous use of danazol. After the long-term treatment, a median of 0.28 (IQ 0-1.2) crisis per year was observed and 18 (40%) patients became totally asymptomatic. The benefit was also observed in the reduction of the severity of the crisis, with a decrease in the need of hospitalization to 8 (13.1%) of these patients, compared with 54 (88.5%) before they were monitored. The side effects associated with the use of the medication were observed in 35 (77.8%) patients submitted to long-term use. The most expressive alterations were weight gain in 29 (64.4%) patients, menstrual irregularities in 18 (56.2%), dyslipidemia in 19 (65.5%) and liver function's alterations in 8 (27.6%) among those patients who did complementary exams. The acceptance of medication was considered good or very good by 32 (71.1%) patients and none of them had to discontinue using the medication because of its side effects.

Conclusion: Danazol is necessary in the treatment of most patients where are limited treatment options available, and its presents well described benefits. There are relevant side effects associated with the use of this medication, which increases the need to use the minimal effective dose. The acceptance of the medication by the patients is considerably high, possibly due to an improvement in the quality of life gained during the treatment.

Adverse effects	Patients (%)
Weight gain	26 (57.8)
Increase of pelage	17 (37.8)
Reduced libido	2 (4.4)
Increase of blood pressure	5 (11.1)
Seborrhea	3 (6.7)
Acne	13 (28.9)
Voice alteration	10 (22.2)
Menstrual irregularity	18 (56.2)
Anxiety	5 (11.1)
Alopecia	4 (8.9)

TP1472 | Rare forms of angioedema in Bulgaria: Experience since 1972. Past and present

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Background: Unawareness about the rare forms of angioedema is wide-spread. Hereditary angioedema (HAE) due to C1 inhibitor deficiency (C1-INH-HAE) is a potentially life-threatening disease. No data has been published about HAE and other rare forms of angioedema in Bulgaria.

Method: Our aim was to identify the clinical characteristics of patients with rare forms of angioedema within a retrospective-prospective cohort study of the Bulgarian population.

Results: The retrospective period 1972-2012 included 202 HAE patients, 111 men: 171 C1-INH-HAE Type 1, 26 C1-INH-HAE Type 2, and 5 non-specified. 86% had positive family history. Mean age of onset was 14.6 year (range, 1-54), while mean diagnosis delay: 10.2 years (range, 1-44). 56 patients were reported dead at a mean age of 36.6 years (34 subjects died from asphyxiation, 77% before establishing diagnosis). 100 patients were lost for follow up (88% C1-INH-HAE Type 1, 8% C1-INH-HAE Type 2). 46 patients continue follow up.

During the prospective (2013-2018) period 85 patients were evaluated: 68 C1-INH-HAE Type 1, 12 C1-INH-HAE Type 2, 2 C1-INH-AAE, 2 nlC1-INH-HAE, 1 InH-AAE. Mean age of onset for C1-INH-HAE is 10.4 years (range, 1-50), mean diagnosis delay: 16.8 years (range, 0-74). Age distribution differs from the general population in Bulgaria, with a smaller percentage of patients among the groups 0-14, and > 65 years. Historically, 18.2% of patients had undergone laparotomy during an abdominal HAE attack; 10.3% had undergone tracheotomy. 4 patients died at a mean age of 55 years, none of them due to HAE. Patients present clinically with peripheral, facial, abdominal, genital, laryngeal edema and neurologic symptoms in 98.8%, 98.7%, 91.9%, 65.7%, 44.3%, and 27.8% of the cases, respectively. Prevalence of C1-INH-HAE in Bulgaria was found 1 in 93 105 people, ranging between 1 in 26 934, and 1 in 174 476 among different administrative regions; No diagnosis is established in 13 regions inhabited by 1.4 million people.

Conclusion: Rare forms of angioedema are underdiagnosed in Bulgaria, although clinical experience exists since 1972. Mean age at disease onset in C1-INH-HAE is in the second decade of life, while mean diagnosis: in the third. History of fatal laryngeal edema is significant; however recently, mortality due to asphyxiation among diagnosed patients is diminished. Common disease presentation (edema localizations) is corresponding to previous reports, while neurologic symptoms related to HAE, are reported by a significant number of subjects.

TP1473 | Hereditary angioedema in a single family with specific mutations in both the plasminogen and SERPING1 genes

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Background: Hereditary angioedema (HAE) is a genetic disease characterized by recurrent tissue swelling which can be lethal when affecting the upper airways, painful when abdominal attacks occur, and which may cause a disfiguring edema in the face and extremities. The most common form is HAE due to complement 1 inhibitor (C1-INH) deficiency. It results from mutations in the *SERPING1* gene, leading to reduced C1-INH function. Rarer forms of HAE with normal C1-INH may arise from mutations in the coagulation factor *F12* gene, but in most cases the genetic background is unknown. Recently, a novel HAE-mutation in the plasminogen (*PLG*) gene was shown. Here we analyzed the different clinical manifestations of HAE in 14 related patients.

Method: We used clinical data, biochemical analysis for C1-INH, C4, and mutational analysis by Sanger sequencing.

Results: Ten patients suffered from swelling of lips or tongue but not of the extremities. The only four patients who displayed gastrointestinal and extremity swelling were three children and their father, who was otherwise not related to the family. Interestingly, the various symptoms could be assigned to two different forms of HAE, caused by mutations in the *PLG* (c.988A>G) and/or *SERPING1 (c.1480C>T) genes.*

Conclusion: This unique finding of two different HAE-specific mutations, one in the PLG gene and the other in the *SERPING1* gene in a large family not only explains the divergent phenotype seen in our patients but also supports a *genotype-phenotype correlation describing abdominal attacks and swelling of extremities as common in HAE-C1-INH but highly unusual in HAE-PLG.*

TP1474 | Hereditary angioedema with gastric expression – atypical presentation

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Case Report:

Background: Hereditary Angioedema (HAE) is characterized by paroxysmal episodes of subcutaneous and submucosal edema, localized and self-limited. It is considered to be an autosomal dominant

pathology caused by a mutation in the C1 inhibitor gene. Although the cutaneous involvement is more common, it often manifests at the gastrointestinal (GI) level, mainly as severe and recurrent abdominal pain, sometimes with associated nausea and vomiting, which becomes a diagnostic challenge and may lead to inconclusive and unnecessary surgical interventions. Considering the reported cases of HAE with expression in the GI tract, involvement of the duodenum and jejunum appears to be more frequent compared to the stomach and colon, which are rarely reported.

Case Report: We report a case of a 51-year-old female, caucasian, to whom the diagnosis of HAE type I was made 7 years before. She presented with episodes of angioedema since the age of 20, apparently with cutaneous involvement only and mainly triggered by trauma, without needing long-term therapy, and medicated during these episodes with aminocaproic acid with rapid improvement. Coincidentally, she presented recurrent episodes of uncontrollable nausea and vomiting since several years ago,1-2 times per month, lasting 5-6 hours and with spontaneous improvement after that. She wasn't able to identify any triggering factor and didn't relate these episodes to the menstrual cycle. This condition was always interpreted by her Gastroenterologist as resulting from a hypotonic gallbladder, and she was treated with domperidone, although without clear improvement of the complaints. In April 2017, a magnetic resonance imaging performed during one of these episodes documented aspects compatible with gastric angioedema, more exuberant at the level of the antrum and pylorus, as well as less expressive angioedema of the duodenum and the initial portion of the jejunum. She started preventive therapy with Danazol 200 mg/day and became completely asymptomatic since then.

Conclusion: The reported case illustrates a rare presentation of HAE with expression in the upper gastrointestinal tract, which can often mimic a gastritis or biliary tract pathology. Clinical suspicion is crucial, even in the presence of a less common condition, in order to carry out the diagnosis and suitable treatment as early as possible.

TP1475 | Systemic mastocytosis (MS) – a deadly case

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Background: Systemic mastocytosis (MS) is a rare pathology of variable prognosis. The clinical manifestations are very heterogeneous and are caused by the proliferation and accumulation of neoplastic mast cells in the tissues and release of its mediators. Treatment involves the prevention of the effects caused by the mast cell mediators and the reduction of the number of mast cells. Most MS presents an indolent and surviving course of decades. Aggressive MS reaches 5% of patients with poor prognosis. The authors describe a case of aggressive MS with a delayed diagnosis, greater than one year.

Method: The authors report a 59-year-old man with recurrent episodes of cutaneous erythema, fever, profuse sweating and lipothymia for more than a year. The patient was more than 10 times to the emergency department, where he was always treated with systemic corticosteroids and antihistamines. In the 5 months before the visit, asthenia, weight loss (10 kg), arthralgia, abdominal pain and diarrhea, nasal obstruction, eye erythema, hoarseness and shortness of breath were almost daily.

Results: Before Allergy visit the patient was submitted to analytical studies, abdominal CT, chest, skull, lung function tests without significant changes, except an erythrocyte sedimentation rate of 38 mm/h and the left adrenal gland slightly increased on abdominal CT. The further study showed a basal tryptase: 160 ug/L(1-15) and in crisis:163 ug/L, catecholamine and metanephrine in 24-hour urine without changes. Because of the suspicion of SM the patient was referred to Hematology. Bone biopsy: diffuse infiltration by pathological mast cells (60-70%), tryptase+, CD25 + , CD117 + , CD2 + ; Negative c-KIT mutation. The diagnoses of SM was performed. The patient was treated with Rupatadine 3-4id, Ranitidine 300 mg id, Montelukast 10 mg id, Paracetamol, Diclofenac, for symptomatic control. Treatment with Cladribine (0.13 mg/kg, 5 days) was started. After 4 cycles the patient presented criteria for progression to myeloproliferative neoplasia: severe anemia (Hgb: 6.2 g/dl) and tryptase > 200 ug/L. He refused transfusional support for religious reasons and died six months after the diagnosis of MS (2 years after the onset of symptoms).

Conclusion: Aggressive SM is a rare situation, so its diagnosis can take several months, with a very important impact on the quality of life and prognosis.

TP1476 | Fracture risk reduction by bisphosphonates in mastocytosis

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Background: Osteoporosis and fragility fractures (FFxs) are frequent manifestations of indolent systemic mastocytosis (ISM). It has been postulated that mast cells directly interfere with bone homeostasis through RANKL-production and other mast cell mediators. Whether standard anti-osteoporotic therapy is sufficiently effective for this patient population with this underlying pathophysiology, particularly on the main clinical outcome, FFxs, has scarcely been investigated. This study evaluates the effect of 5-year bisphosphonate treatment on the number and risk of FFxs, on bone mineral density (BMD) and on bone resorption in ISM patients in daily clinical practice.

Method: Seventy-six ISM patients who had received bisphosphonates because of osteoporosis and/ or fragility fractures were analysed retrospectively. Primary outcome was fracture incidence during 5-year bisphosphonate treatment. Fractures were recorded

by vertebral fracture assessment or X-rays of thoracolumbar spine, medical records and a questionnaire. Thirty patients had a complete fracture dataset with baseline and 5-year measurements. Their observed fracture risk was compared to their predicted risk had they remained untreated with anti-osteoporotic drugs by using the MastFx score. Secondary outcomes were change in BMD Z-score and serum collagen C telopeptide (sCTx) Z-score.

Results: Twenty-one vertebral FFxs were detected in 8 of 30 patients, no non-vertebral FFxs were detected. Observed fracture risk was 26.7%, which was lower than the predicted 5-year risk (33.5% to 38.5%) based on MastFx scores. Fracture risk was particularly high in patients with a history of FFxs, 66.7% (predicted risk 51.6% to 53.0%, suggesting reduced effectiveness in this subpopulation). Lumbar BMD Z-score significantly increased from median -2.20 (IQR -2.80 to -1.50) at the start of treatment to -1.50 (-2.30 to -0.60) at 5-year follow-up ($P < 0.001$, n = 27). sCTx Z-score decreased from median (IQR) 0.71 (-0.59 to 2.39) to -0.95 (-1.30 to -0.16) ($P = 0.008$, n = 15).

Conclusion: Five-year bisphosphonate therapy lowers FFx risk in ISM patients, increases BMD and decreases sCTx. Nevertheless, risk and number of fractures remains high, particularly in patients with a history of FFxs, which underlines the high burden of disease and hence the need for prospective studies on bisphosphonates and other anti-osteoporotic drugs in this population.

TP1477 | Pulmonary and cardiovascular symptoms in patients with mastocytosis

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Background: Mastocytosis is a group of rare diseases characterized by excessive growth of mast cells in skin, bone marrow, liver, spleen, lymph nodes. Signs and symptoms result mostly from mast cells mediators and mast cells organ infiltration. Pulmonary and cardiovascular localization of mastocytosis is extremely rare and in most instances have not been substantiated with pathologic confirmation.

Method: Evaluation of cardiovascular manifestation included morphology, serum level of troponin T, electrocardiography (ECG) and echocardiography. Evaluation of pulmonary manifestation included spirometry, diffusing capacity of the lung for carbon monoxide (DLCO) and evaluation for mastocytosis included bone marrow biopsy and serum total tryptase measurements. Patients with impaired DLCO had performed high resolution computed tomography.

Results: In the study there were 108 patients - 70 women and 38 men between 19 and 74 years old (the average age was 47). There were 4 patients (3.7%) patients with MCAS, 21 (19.44%) with MPCM, 76 (70.37%) with ISM, 4 (3.70%) with SSM, 2 (1.85%) with ASM and 1 (0.94%) patient with MCL. Troponin levels was within the normal range in all patients. Three patients had lowered the ejection fraction (EFLV = 23%; 56%, 59%). No one patient had obturation and restriction. And impaired DLCO (under 75% of predicted value) had 13 patients (12%). 9 patients (8.3%) were treated due to asthma, but dyspnea was presented among 37 patients (34.3%). Chest pain have been reported in 22 patients (20.4%). 24 (22.2%) patients were treated due to hypertension, 11 (10.2%) – diabetes mellitus and prediabetes, 7 (6.5%) – arrhythmias.

Conclusion: All patients with systemic mastocytosis should be systematically evaluated for the presence of impairment of long diffusion. We plan further studies to diagnose the reason for the impairment DLCO.

TP1478 | Coexistence of mastocytosis in the skin with vitiligo (fortuity or coincidence?): A russian center case series

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Background: Adult mastocytosis with skin involvement is characterized by accumulation of mast cells (MCs) in various organs and is claimed to be associated with c-KIT mutation. Vitiligo is a depigmentation disorder due to the loss of functioning melanocytes. Both conditions are rare and their coexistence has not been described. Vitiligo is known to be associated with autoimmune disorders, primarily thyroid diseases and alopecia areata. However, reports on mastocytosis- and vitiligo-associated cutaneous disorders are missing.

Method: Two (5%) of 42 patients with MIS, seen at our Department over a 4-year period, suffer from the coexisting non-segmental vitiligo (NSV). The other 2 (5%) patients were diagnosed with halo nevus (HN), known to be a predisposing factor for vitiligo. Diagnosis MIS was confirmed clinically in 3 cases by the evidence of typical brown-to-red maculopapules with positive Darie sign and histologically (toluidine blue staining) and immunohistochemically (CD117 immunostainig) in 1 case with minimal rash. One patient with extended NSV- and MIS-lesions was treated with psoralen-ultraviolet A phototherapy (PUVA).

Results: All patients with NSV and HN were 24 to 38 aged females. The age of MIS onset varies from 11 to 33 years, NSV onset from 7 to 34 years and HN onset from 0 to 30 years. In 3 cases both diseases occurred almost simultaneously within a 5-year period. No connection between the priority of the order of development of one or another disorder was identified. A good response on PUVA-therapy was demonstrated with partial repigmentation improvement of vitiligo-lesions and decrease in the number of mastocytosis-related maculopapules.

Conclusion: MIS patients are at higher risk of vitiligo development. Melanocytes are claimed to be the main affected cells in vitiligo, but mast cells, keratinocytes, fibroblasts can also be involved and affect their function. Aroni et al. identified increased number of MCs in vitiligo patches, what is common for mastocytosis. In vitiligo high number of MCs and vascular endothelial growth factor (VEGF) expression may increase vasodilatation and angiogenesis being described in autoimmune disorders and mastocytosis. Angiogenesis and VEGF are also known to promote the growth of neoplastic cells in malignancies. The etiology of these findings is not fully understood and requires further investigations to develop new treatment options with a more prolonged result.

TUESDAY, 4 JUNE 2019
TPS 49
DRUG ALLERGY, TESTING AND MISCELLANEOUS

TP1480 | Basophil activation testing is useful in children allergic to neuromuscular blocking agents

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Background: Neuromuscular blocking agents (NMBA) are frequent cause of immediate reaction during anesthesia in children. Basophil activation testing (BAT) to NMBA has been applied as useful additional test in adult patients, but data on children population is missing.

Method: Nine children (3 girls, 6 boys) have been investigated because of suspected NMBA allergy between 2010- 2017. Four children received vecuronium, two child received mivacurium, two cisatracurium and one atracurium. Skin testing (ST) with NMBA and basophil activation test (BAT) have been made. BAT assessed analyses of basophil CD63 surface expression in association with stimulation index (SI).

Results: Six children had positive skin testing results to multiple NMBA (one child to six NMBA, one child to five NMBA, two children to four NMBA, two children to three NMBA). Two children had positive skin test results to one NMBA. One child had dermographism.

Six children (78%) had positive BAT results to NMBA. Two children had positive BAT to given NMBA and four to others. One child had positive BAT to four NMBA, two children to three NMBA, two children to one NMBA and one to two NMBA.

Conclusion: BAT is a useful additional test in children allergic to NMBA. BAT showed lesser pattern of cross reactivity in comparison to skin testing results.

TP1481 | Drug allergy in children – a referral to pediatric allergy consultation

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Background: Drug allergy (DA) is an adverse drug reaction that results from a specific immunologic response to a medication. In children, the major obstacle to diagnosis is differentiation between DA reactions and maculopapular drug eruptions from viral exanthema, very common in this age group. However, DA may also cause serious or even life-threatening reactions, which emphasizes the need to confirm the correct diagnosis.

Method: Retrospective observational study which included children referred to pediatric allergy consultation in a second-level hospital with suspected DA during the year 2018.

Results: 52 children were included in the study, which represented 82 medical appointments during the year 2018. 55.8% (n = 29) were male with a median age of 3 years. 38.5% (n = 20) had an allergic disease and 40.4% (n = 21) had a family history of atopy. Most cases were referred by doctors in the emergency department (63.5%, n = 33). The majority of drugs suspected of causing allergy were antibiotics (82.7%; n = 43), 97.7% (n = 42) of which were beta-lactam, and non-steroidal anti-inflammatory drugs (NSAID) (19.2%; n = 10). One case had suspected allergy to both drugs. 31 children (59.6%) underwent a drug provocation test (DPT), bringing to a total of 37 tests. Only 16.2% of these tests (n = 6) were positive. DA was confirmed in 8 children (15%), half to beta-lactam antibiotics and half to NSAIDs.

Conclusion: As reported in other studies, beta-lactam antibiotics and NSAID were the drugs responsible for most of the referrals to pediatric allergy consultation probably because they are the most prescribed in pediatrics. As DPTs are the gold-standard for drug allergy diagnosis, it was expected that most children were tested, but the need to carry out the DPT under appropriate clinical conditions postpones these tests especially in early childhood. In our study as reported in literature reviewed, the majority of children didn't have drug allergy.

TP1482 | Drug induced enterocolitis syndrome (DIES): A clinical entity which deserves more awareness

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Background: Enterocolitis syndrome is a potential severe non-IgE mediated hypersensitivity reaction, characterized by gastrointestinal symptoms and a systemic inflammatory response which may progress to a state of hypovolemic shock. To date, the most commonly reported triggers for enterocolitis syndrome are food proteins (food protein induced enterocolitis syndrome (FPIES)). However, enterocolitis syndrome induced by drugs (DIES) has been previously described and deserves more clinical awareness.

Objective: By describing a case report of DIES and reviewing literature on DIES we aimed to define diagnostic criteria for DIES, which

Diagnostic criteria for patients presenting with possible DIES	
Major criteria:	Minor criteria:
Vomiting in the 1- to 4-h period after ingestion of the suspected drug and absence of classic IgE-mediated allergic skin or respiratory symptoms	1. A second episode of repetitive vomiting after ingestion of the same drug 2. Repetitive vomiting episode 1-4 h after ingestion of a different drug 3. Extreme lethargy with any suspected reaction 4. Marked pallor with any suspected reaction 5. Need for emergency department visit with any suspected reaction 6. Need for intravenous fluid support with any suspected reaction 7. Diarrhea in 24 h (usually 5-10 h) after ingested drug 8. Hypotension 9. Hypothermia

The diagnosis of DIES requires that a patient meets the major criterion and > 3 minor criteria. If only a single episode has occurred, a diagnostic OFC should be strongly considered to confirm the diagnosis

can help the clinician to recognize and diagnose DIES and can also be used for investigative purposes.

Method: We describe a case report of a four year old boy who was referred to our pediatric allergy clinic because of suspicion of DIES by amoxicillin. The diagnosis DIES was confirmed by a positive oral challenge with amoxicillin. In addition, a comprehensive literature search on DIES was performed.

Results: A total of 2 articles in which DIES has been reported were identified. Because of the limited number of articles found, we decided to propose diagnostic criteria based on Nowak's criteria for FPIES (Table 1).

Conclusion: DIES is a non-IgE cell mediated drug allergy that can be severe and lead to shock. We propose diagnostic criteria for DIES in order to improve both clinical and scientific knowledge.

TP1483 | Hypersensitivity to analgesic/non-steroidal anti-inflammatory drugs: A retrospective study in a pediatric cohort

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Background: The hypersensitivity (HS) reactions to Analgesic/Non-Steroidal Anti-Inflammatory drugs (A/NSAID) in the pediatric population are not well characterized and its EAACI/ENDA classification have limitations.

Objectives: To analyze the clinical patterns of the HS reactions to A/NSAID referred to a pediatric drug allergy outpatient clinic (PDA-C).

Method: Retrospective study of the population admitted in our PDA-C with probable HS reaction to A/NSAID in the last 4 years. Demographic and clinical data and the results of the skin tests (ST) and/or oral provocation tests (OPT) performed were collected from patients' medical record.

Results: There were included 26 patients (31 reactions) with probable HS reaction to A/NSAID (median age [Q1, Q3] of 10 [6; 15] years, 58% females, 42% atopic, none with asthma nor chronic urticaria). The reactions that motivated the admission in PDA-C were immediate in 35% of the cases (2 anaphylaxis, 5 angioedema, 2 urticaria+angioedema, 2 urticaria) and in 65% delayed reactions (14 urticaria, 4 maculopapular exanthema, 1 mouth sores, 1 vomiting). In the 2 patients with anaphylactic reactions, OPT with an alternative A/NSAID were performed (1 tramadol, 1 celecoxib) being both negatives. In the remaining 24 patients, ST were performed in 7 patients (3 paracetamol, 1 ibuprofen, 1 fentanyl+rocuronium+tramadol, 2 beta-lactams) and in all 24 patients, diagnostic OPT were made (27 with A/NSAID and 2 with beta-lactams). All the ST were negative and the OPT confirmed the diagnosis in 5 patients and excluded it in 19. The 5 patients with confirmed A/NSAID HS were admitted for immediate cutaneous reactions to ibuprofen and in the OPT all of them developed similar cutaneous manifestations. The 19 patients in which HS was excluded (5 paracetamol, 12 ibuprofen, 1 tramadol, 1 nimesulide), 89% were admitted due to cutaneous manifestations (68% delayed), 47% had a concomitant infection and 47% were atopic.

Conclusion: Most of the reactions to A/NSAID admitted in our PDA-C were cutaneous delayed reactions. The OPT confirmed HS reactions to A/NSAID in 27% of the cases, all admitted for immediate reactions. OPT with acetylsalicylic acid was not performed; therefore, cross reactivity was not proved, which is a limiting factor of the study. Our data suggest that HS reactions to A/NSAID drugs in the pediatric population have different characteristics from the adults' reactions to A/NSAID, such as different phenotypes.

TP1484 | Systemic mastocytosis in a 5 year old child presenting with hypovolemic shock, succeeded by severe anaphylaxis to fentanyl

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Case report: Mastocytosis is characterized by the clonal expansion and accumulation of mast cells (MCs) in different tissues and organs.

In children, cutaneous mastocytosis, or typical maculopapular cutaneous lesions (TMCL/urticaria pigmentosa), is the most common form of mastocytosis, with a prevalence of 13 in 100.000, and resolution in many in puberty. Systemic mastocytosis (SM) is very rare in children. However, it is more likely in children with a persistent serum tryptase level of > 20 ng/mL, or those with symptoms of explosive diarrhea, syncope, as well as recurrent anaphylaxis reactions. Precautions are taken for procedural anesthetics if SM is suspected. In these cases, histamine releasing opioids, like morphine, are preferably replaced by fentanyl or any other synthetic opioid.

Case presentation: A 5 year old boy was referred to our hospital. At age six months, the patient was referred to a dermatologist for lesions on his forehead, consistent with TMCL, confirmed by a skin biopsy. During his entire life, he frequently suffered from diarrhea. At age three he was seen by a pediatrician for failure to thrive. At this point, serum tryptase was 42.6 ng/mL. The consulted gastroenterologist concluded there was no SM. Tryptase was 47.1 ng/mL. At age five, the patient suffered from an anaphylactic shock following diarrhea for which he had to be resuscitated. During transfer to pediatric intensive care, morphine was administered intravenously, which triggered severe hypotension. Therefore, renewed intubation was performed using fentanyl provoking again severe hypotension. Tryptase rose to > 200 ng/mL. A few weeks later, without any complication, bone marrow biopsy (BMP) was performed under general anesthesia using propofol and ketamine after administration of H1 and H2-blockers intravenously. BMP revealed abnormal morphology of MCs (>25% spindle shaped), an activating mutation at codon 816 of *KIT*, and the expression of CD25 in MCs, but no aggregates of > 15 mast cells (major criterion). Hereby, meeting all minor criteria for SM. In follow-up the patient is doing well with H1 and H2-blockers combined with nalcrom.

Conclusions: SM should be considered in all children with a persistent serum tryptase > 20 ng/mL. In this case, severe delay was most likely due to lack of knowledge. Anaphylaxis to synthetic opioids is rarely seen, but possible and all anesthetics should be administered in a highly controlled setting in children with SM, preferably after premedication.

TP1485 | A six months old female infant with erythema multiforme: A case report

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Case Report:

Introduction: Erythema Multiforme (EM) is a rare, immune-mediated skin disease characterized by the abrupt onset of typical and/or atypical target lesions, predominantly observed in young adults. The disease is very uncommon during childhood, with only few cases reported in infants. It is usually due to infection or medications, and it can be classified in minor or major (severe mucosal involvement and systemic symptoms).

Typical lesions have at least three distinct zones, an epidermal damage in the centre and usually heals without sequelae. The diagnosis is made clinically and differential diagnosis can be made with urticaria, vasculitis, Stevens-Johnson syndrome, Kawasaki and Lupus erythematosus.

Case description: Female patient, six months old, presented acute, fixed, papular target lesions on her skin, with no itching, mucosal involvement or systemic symptoms. They had variable size and were observed on the limbs. There was no history of medication or infection (including the mother, still breastfeeding). The patient had been previously assisted by two pediatricians who prescribed topical corticosteroids associated with oral first generation antihistamines, with no improvement. As initial investigation, virus and bacterial serologies were required. Skin hydration was established, with frequent reassessments. No oral corticoid or specific therapy to an infectious factor were initiated as there was no clinical signs of EM major or infection. After three days, the lesions were clearer and serologies were positive to Herpes Simplex Virus (HSV) IgG (1.19). Within two weeks, lesions were completely gone and serologies came positive to HSV IgG (1.23), IgM (2.05) and Herpes Zoster Virus IgM (1.77).

Conclusion: EM lesions in infants are poorly recognized by physicians, due to its low incidence and several differential diagnosis. Misdiagnosis can result in inappropriate medications, with side-effects, and undiagnosed infections that can evolve into serious complications. Therefore, we believe pediatricians should consider EM as a differential diagnosis to mucocutaneous lesions in children. The use of corticosteroids as treatment to EM has generated controversy in literature, being generally used in EM major. In this case we found to be possible to postpone its use until further reassessment, considering EM minor has a self-limited pattern and the patient's revaluation was ensured. The patient′s mother has signed a written informed consent for this publication.

TP1486 | When the sun is no fun: Solar-induced? Angioedema in pediatrics

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Case report: A 7-year-old boy was referred for a one year history of intermittent angioedema affecting mainly his hands and/or feet occurring every few months. Accompanying symptoms included burning and tingling at the site, sometimes with a petechial rash, and a low grade fever which did not resolve with ibuprofen. His past medical history was unremarkable. His family history was significant for his maternal grandmother having systemic lupus erythematosus (SLE).

After assessment by his Pediatrician and Rheumatologist he was referred to Allergy for angioedema. He was initially diagnosed with viral-induced angioedema, with considerations of NSAID hypersensitivity and hereditary angioedema. An exposure diary subsequently revealed an association of his rash and angioedema with prolonged sun exposure which broadened the differential diagnosis to include erythropoietic protoporphyria (EPP).

His physical examination, routine chemistry and CBC with differential were normal. Given the family history of SLE, an assessment revealed negative ANA, anti-Ro and anti-La antibodies. An evaluation for hereditary angioedema revealed normal C1 esterase inhibitor and C4 levels. Serum free erythrocyte protoporphyrin (FEP) was elevated at 18.7 micromoles/L (0.4-1.0), which was highly suggestive of EPP. Genetic analysis demonstrated positivity for two variants of the FECH gene.

EPP is a photodermatitis disorder and belongs to a group of disorders characterized by abnormalities in the heme biosynthesis pathway. Although rare, EPP is the most common porphyria in childhood and can have a profound impact on quality of life and long-term clinical effects, including solar induced cutaneous pain, scarring and pigmentary changes, and a risk of severe liver damage.

EPP has a known diagnostic delay as patients may have no immediate objective visible skin changes after sun exposure, despite a sensation of burning and tingling. In pediatrics, the chronic pigmentary skin changes may have not yet occurred. However, most patients with EPP do experience hours to days of swelling with solar exposed skin and can be referred to Allergy for a concern of angioedema. Importantly, it is necessary for Allergists to consider EPP in the differential for angioedema and carefully elicit any relationship of skin symptoms to solar exposure to allow for the accurate diagnosis and appropriate management.

TP1487 | Features of the clinical course of atopic dermatitis related to the types of breeds of microorganisms in young children

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Background: The skin is an ecosystem that serves as a barrier of specific protection. The constant microbiome of the skin and keratinization processes are responsible for the constant updating of the stratum corneum. Literature reviews show that structural pathology in epidermis in atopic dermatitis (AD) leads to local immune system chronic activation and susceptibility to fungal and bacterial infections. Aim was to investigate the clinical course of AD related to the types of breeds of microorganisms in young children.

Method: 58 patients (age 3 months - 3 years old) with an exacerbation of AD of various severity were included into the study. Bacteriological methods and culturing (Sabouraud agar, Sabouraud agar with levomycetin) were used for identification of the breeds. pH level of the skin was also measured.

Results: In 32 patients (55.2%) treatment with moisturizers and elimination diet was ineffective. 28 children among them had non-typical for AD skin elements due to its morphology with signs of infection. Along with dryness, lichenification, redness and exacerbations there were determined scalping spots with raised edge, double contour, clearly delimited with circumferential forms and fractures with blood secretion. All these patients had changed pH levels (<5.5; >5.8). It was found that among them 26 patients with non-typical skin elements had excessive quantity of both bacteria and fungus inhabiting the skin (S.aureus $>10^5$ (n = 14), St. haemolyticus $>10^5$ (n = 7), Chryseobacterium sp. $>10^5$ (n = 2), Horodendrum compactum (n = 2), Hormodendrum pedrosoi (n = 1), Candida albicans (n = 7), Candida nonalbicans (n = 3)). The severity of the course of AD correlated with pH changes and skin infection (<0.05).

Conclusion: 45% cases of routine culturing revealed bacterial (80.8%) and fungus (50%) infection in young children with AD which was supported with abnormal pH levels of non- typical elements on the skin.

TP1488 | Laronidase hypersensitivity and desensitization in type I mucopolysaccharidosis: A case report

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Case Report:

Background: Mucopolysaccharidosis-I (MPS-I) is a rare disorder, resulting from the deficiency of lysosomal alpha-L-iduronidase enzyme. Untreated patients have a lower life expectancy and higher morbidity. The enzyme replacement therapy(ERT) with laronidase has been approved for MPS-I treatment since 2003. We describe the youngest case of a MPS-I patient with hypersensitivity to laronidase, who was successfully treated with a three bags, 12 steps rapid desensitization protocol.

Case report: A 5-yr-old male was referred for hypersensitivity reactions during ERT with laronidase. He was diagnosed with MPS-I when he was 3 yr-old. He started ERT with laronidase(11.7 mg/wk). He received uneventful infusions weekly during 2 years. At 2 years, 60 min after starting the procedure(infusion rate:80 ml/h), he experienced hives in arms, back, lip swelling and increase in corporal body temperature without respiratory, or cardiovascular symptoms. The infusion was stopped, and the patient was treated with dexchlorpheniramine, and the symptoms improved. Same symptoms were observed during next infusion of ERT one week later. A skin prick test with undiluted laronidase(0.58 mg/ml) was positive with a 5 mm-diameter wheal as compared with the negative control. A three bags laronidase desensitization protocol was elaborated. The patient was pre-medicated with ranitidine,

methylprednisolone, dexchlorpheniramine and montelukast. The desensitization was done in the intensive care unit. He needed to add new doses of methylprednisolone and dexchlorpheniramine during infusion, because at first attempt repeated a reaction. Afterwards, the patient was treated for 7 months weekly without reactions.

Discussion: After establishing the nature of the hypersensitivity reaction to laronidase, desensitization was indicated, as the patient was in need of the medication, and there was high risk for anaphylaxis. Protocols for desensitization vary according to the nature of the reaction, the drug involved, and the route of administration. Based on other protocols, we elaborated a new successful laronidase protocol with three bags and 10 steps.

TP1489 | The current state of infant skincare methods at obstetrics departments and maternity hospitals

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Background: Recent studies have reported that maintaining adequate skin-barrier function from an early age, including infancy, may help reduce the risk of onset and slow the progression of atopic dermatitis, bringing about greater awareness of the importance of skin moisturization from the earliest stages of life. However, results of a survey about skincare conducted in Fukuyama, Hiroshima, to parents who brought their children in for 18-month checkups revealed that only a few of the parents understood correct skincare methods.

Method: A survey questionnaire about bathing guidance was administered to midwives at 8 sites in Fukuyama in April and May of 2018, comprising obstetrics departments and maternity hospitals where childbirth support services were available. Participants were asked questions about (1) bathing methods, (2) washing soaps, (3) moisturizing methods, (4) skincare, and (5) their confidence in skincare methods.

Results: Valid responses were collected from 48 midwives across 8 facilities; their mean age was 37.5 years. To the question about what they use to wash infants during bathing, 23% reported their hands, 62% pieces of gauze, and 10% towels. To the question about whether they use soap during bathing guidance sessions, the largest number reported they use foaming soap for the head and body, and many reported that they use nothing for the face. Regarding confidence in skincare methods, many reported that they do not have high confidence in their knowledge.

Conclusion: Improving the clinical care environment such that parents can be properly informed about skincare methods, either prior to childbirth or soon after, may increase the possibility of reducing the risk of infant skincare problems. Cooperation between obstetrics departments and maternity hospitals is also important and should be discussed in the future.

TP1490 | Chronic urticaria: A spanish pediatric cohort

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Background: Pediatric chronic urticaria (CU) is a rare and scarcely known disease, associated with significant quality of life impairment. Often angioedema (AE) is associated. We describe the pediatric CS cohort of our Hospital.

Method: This is a retrospective study set at the Son Espases University Hospital. All patients diagnosed in last two years, with CU and under 15-years-old at diagnosis were included, excluding patients with acute urticarial.

Results: Twenty-nine patients were included, 58.6% female. Mean age at first symptom was 6.6 years. The average diagnosis delay was 13.6 months. Family history of atopy was reported in 62% of cases. Family history of CU was not frequent (10.7%). Personal history of atopy (55%) and dysimmunity (17.2%) were observed. A lot of CU-crises included AE (41.3%) and 6.8% presented as isolated AE. A trigger was found in 45%, mainly physical.

The majority of CU was controlled by single (60%) or double dose (17.2%) of H1-antihistamines. We use quadruple dose in 6 patients (5 of them were refractory cases and they needed omalizumab). We had 1 case of thyroiditis who was controlled with minimum dose of levothyroxine, and 1 case of Solar Urticaria who was treated with desensitization with UVA rays and had a partial response.

Conclusion: As in adults, pediatric CU was more frequent in females and associated with personal/familial features of atopy. Therapeutic management is extrapolated from adult guidelines. Specific pediatric CU assessment tools for disease activity and quality of life are needed to lead the prospective studies that will help define specific pediatric management.

TP1491 | The importance of measuring the concentration of nitrous oxide in exhaled air for epidemiological phenotyping of asthma in children

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Background: Nitric oxide in exhaled air (FeNO) is a marker of the eosinophilic inflammation of the respiratory system, widely used for clinical purposes. It is less frequently used in epidemiological studies. The aim of the study was to evaluate the differences of FeNO

levels in children with chronic respiratory conditions, including asthma, under epidemiological study conditions.

Method: Children were examined using the ISAAC questionnaire and the FeNO NIOX MINO device for FeNO measurement. Children were divided into 3 groups: no respiratory symptoms – healthy (H); with respiratory symptoms but without an asthma diagnosis – symptoms (S); and children with diagnosed asthma (As). In addition, allergy symptoms (Al +/Al-) were taken into account. FeNO was categorized as normal vs high at the cutoff of 19 ppb.

Results: There were 441 children (50.3% boys and 49.7% girls) aged 6-10 years examined. The largest group were H children (78%) then S (14%) and children with As (8%). FeNO values were different between the three groups [H: 14.1 ± 9.8 ppb, S: 19.2 ± 17.8 ppb, As: 22.2 ± 19.9 ppb, (P = 0.002)]. Allergy was found in 16% of children. FeNO levels were higher in those with allergic disease [Al+ FeNO was 19.1 ± 15.4 ppb, Al− FeNO was 14.8 ± 11.7 ppb, (P = 0.02)]. The presence of allergy was important for FeNO values only in children with asthma: FeNO As+/Al+=18.2 ± 14.9 ppb and FeNO As+ / Al− = 17.4 ± 15.0 ppb, P = 0.04. In addition, the presence of allergy in children with asthma was a predictor of elevated FeNO values (OR = 6.30 95% CI: 1.27-31.12).

Conclusion: Higher FeNO concentrations occur in children with asthma. In this group, the presence of allergy was associated with higher FeNo values This knowledge can be used in epidemiological phenotyping of asthma in children.

TP1492 | Allergy to chironomid larvae in a child owing an exotic pet

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Case report:

Background: Red midge larvae (Chironomus thummi thummi), an insect belonging to the Dipteria orden, is especially found in wetlands. Allergy to this larva has usually been described after occupational and recreational exposures. It is also commercialized as fish food and due to the increase of exotic pets over the last years, allergy to chironomid larvae has also been described in other situations.

Case Report: We present the case of an 11-year-old boy with a history of seasonal allergic rhinoconjunctivitis and mild intermittent asthma due to olive and grass pollens. He reported sneezing, conjunctivitis, and facial wheals and edema immediately after feeding his triton with chironomid larvae for the first time. The reaction subsided after treatment with corticosteroids and antihistamines.

Skin prick tests (SPT) with chironomid larvae (*Chironomus thummi thummi)* extract (3 mg/ml*)* was positive *(13 mm).* SPT with a mosquito *(Aedes communis)* and cockroach (*Blatella germanica*) were also positive. Negative results were found in SPTs to house dust mite, *Anisakis simplex*, mussel, shrimp, bee and wasp. Total serum IgE was 436 kUA/L and specific IgE was strongly positive to *Chironomus thummi thummi*,(189 kUA/L), and low to cockroach (0.44 kUA/L) and horsefly (0.45 kUA/L).

The chironomid larvae extract was resolved with SDS-PAGE and an IgE immunoblotting was performed under non-reducing conditions. The patient's serum showed recognition of bands ranging from 10 to 15 kDa, that matched those of the monomeric form of the chironomid hemoglobin, the major allergen previously identified. No cross-reactivity between chironomid larvae and cockroach was observed in ELISA and Immunoblot-inhibition tests. A basophil activation test using CD63 as a marker for activated basophils was performed with *Chironomus thummi thummi* extract. Positive results were found at all concentrations tested (ranging from 3 mg/ml to 0.3 µg/ml) with a maximum activation of 64.37%.

Conclusion: We present the first case of allergy to *Chironomus thummi thummi* in a child exposed to these larvae as food for a triton pet. With the increased presence of fish and amphibians at homes as pets, allergy to Chironomid larvae may increase and appear in new patients' groups as children.

TP1493 | Internet use habits of parents having children with allergic diseases

Kulhas Celik I[1]; Buyuktiryaki B[1]; Capanoglu M[2]; Batmaz SB[3]; Can D[4]; Usta Guc BE[5]; Civelek E[1]; Toyran M[1]; Dibek Misirlioglu E[1]; Kocabas CN[6]

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Background: Internet and social media have various areas of use, one of which is health communication. Internet and social media are not only vehicles for obtaining information and sharing health-related experiences, but also play a role in decision-making as individuals collect information and recommendations on health issues, health care centers, and physicians.

Method: This study was conducted by a questionnaire filled by the parents having children with allergic diseases who applied to the pediatric immunology and allergy outpatient clinics of 6 centers (Ankara, Erzurum, Tokat, Balikesir, Adana, Mugla) between March 2017 and July 2017.

Results: Among the 704 participants, mean age was 34.2 ± 4.7 years, 70% were women. 70% of the participants stated that they sought on internet about their children's complaints before applying to a doctor. 20.7% of the participants stated that they use internet daily

and 25.5% stated that they use a few times a week. Of the participants, 53.2% reported that Internet is always useful. Governmental institution websites (34.7%) were the most preferred source for information. 64.4% of the parents found Internet sources through Web searches by themselves. They sought information about prevention of allergy (56.3%), doctor and hospital advices (50.6%) and allergy diagnostic tests (48.7%). 53.6% of the participants stated that advices on Internet and doctor's advices are sometimes incompatible and while 67% accepted the doctor's information as correct, 27.9% stated that they trusted on the information on Internet. In addition, 53.6.7% stated that they always or most of the time give advices to other patients and their families on the Internet. The most common advice was doctor advice (%72.3).

Conclusion: As the use of internet is an unavoidable reality today, presence of websites directed by healthcare professionals might be helpful in order to provide accurate information and appropriate recommendations to patients and their parents. Another possibility is to officially monitor these sites and introduce a certification process to ensure the accuracy of health information contained therein to prevent potential adverse effects on patients' wellbeing.

TUESDAY, 4 JUNE 2019
TPS 50
FOOD ALLERGY IN CHILDHOOD

TP1494 | Incidence, triggers, symptoms and treatment of anaphylaxis in a pediatric hospital in São Paulo, Brazil

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Background: Anaphylaxis is a dramatic expression of systemic allergy. Through epidemiological studies, it is possible to better investigate the disease, triggers, cofactors and prevention. However, few studies have evaluated these aspects of the disease among Brazilian children.

The purpose of this study was evaluate the incidence of anaphylaxis cases in the emergency room of a private pediatric hospital in the city of São Paulo, Brazil and study associated factors, such as symptoms, triggers and treatment.

Method: This was a cross-sectional, retrospective and observational study based on the medical record of pediatric patients (0 to 18 years of age) seen at the emergency unit of the Sabará Children's Hospital during the years of 2017 and 2018. Cases of anaphylaxis were searched based on a list of related diagnoses (ICD-10) and then all medical records were individually reviewed by an allergist doctor. Possible cases were defined by the presence of anaphylactic symptoms in at least two systems. Possible cases were considered probable cases when the medical history was compatible and indicative of anaphylaxis.

Results: In 2017 (105 523 medical visits) and 2018 (102 133 medical visits) the incidence of possible cases was 0.046% and 0.041%, respectively, and the incidence of probable cases was 0.015% and 0.014%. Among the 30 probable cases (53% of girls, median age of 5 years old), foods were the most common triggering factor (50%), followed by unknown trigger (33%) and drugs (13%), based on clinical history. 27% of the cases had an associated cofactor and 20% had a previous history of anaphylaxis. Cutaneous symptoms were observed in all cases (mainly urticaria), respiratory symptoms in 70% (mainly cough) and gastrointestinal symptoms in 50% (mainly vomiting). No cardiovascular shock was observed, and no death occurred among these cases. Intramuscular adrenaline was administrated in 43% of the cases, antihistamine in 97% and systemic corticosteroid in 87%. 33% of the cases were maintained in observation at the hospital for at least 6 hours. At discharge, 40% were referred to an allergy specialist and 14% received self-injecting adrenaline prescription.

Conclusion: The incidence of probable cases of anaphylaxis was low among children and adolescents and foods were the most implicated trigger. The use of intramuscular adrenaline was still lower than recommended. Education programs should be implemented to improve recognition and treatment of anaphylaxis.

TP1495 | Regional audit of paediatric anaphylaxis management in the midlands: Are we following national guidance?

Dhesi A; Maria R; Bates H; Seager E; Stiefel G; Dawson T; Darwood I; Holt A; Ferdinand D.; Goel C.; North J.; Atkinson M.; Karanam S.; Makwana N

Sandwell and West Birmingham Hospitals NHS Trust, Birmingham, United Kingdom

Background: Anaphylaxis is an acute, potentially fatal systemic reaction. Our aim was to evaluate compliance to national guidance across regional UK hospitals.

Method: We performed a retrospective analysis of all children aged 0-16 years, with a coded diagnosis of anaphylaxis in hospitals across the Midlands between 2014 to 2016. A proforma was compiled and data were collected from clinical records.

Results: 110 clinical records were available. 67 were considered as true anaphylaxis. The median age was 9 years. Presenting symptoms included pharyngeal/laryngeal oedema (61%), bronchospasm with tachypnoea (72%), circulatory collapse (24%) and skin/mucosal changes (85%). 96% of clinical notes had the preceding causative circumstances documented and 91% time of onset of symptoms. The suspected triggers were nuts (52%), other foods (16.5%) and drugs (4.5%). Other foods included sesame (3%), egg (3%) and prawns (1.5%). In 25% the exact culprit was unknown. 34% of patients had a previous history of an anaphylactic reaction, 42% asthma and 43% eczema. 75% received intramuscular (IM) adrenaline of which 72% was administered pre-hospital. 49% received nebulised salbutamol, 87% antihistamine and 76% steroids. 10% of patients needed fluid resuscitation.

At discharge, 75% were referred to the local allergy service. 61% were provided with an autoinjector but only 71% of them had training on its use documented in their notes. A further 10% of patients already had access to an appropriate autoinjector. 55% were provided with information about the signs and symptoms and what to do in the event of anaphylaxis. 13% had recorded provision of information about biphasic reactions but only 7% were provided with information about patient support groups on discharge. Of the patients who had a suspected trigger, 42% had documented advice regarding trigger avoidance. A written management plan at discharge was only documented in 16% of patients.

Conclusion: The failure to recognise anaphylaxis may explain why only 75% patients received IM adrenaline. Conversely, 46% of excluded patients which were not considered to have true anaphylaxis received IM adrenaline, highlighting the need for ongoing education for health professionals. There is a high standard of history taking but emphasis needs to be placed on documentation, counselling, adrenaline autoinjector training and written emergency plans before hospital discharge.

TP1496 | Allergen sensitization pattern of children with allergic diseases: Single center experience

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Background: Allergic diseases are an important health problem increasing in prevalence. An important part of the treatment is to avoid susceptible allergen. Therefore, it is important to identify allergen sensitivity. Skin prick tests are minimally invasive, reliable and sensitive tests used for this purpose.

Method: In this study, we have evaluated the patients who were diagnosed with allergic disease and undergone skin prick test on January 2013-February 2015.

Results: A total of 4885 patients were included. The mean age of the patients was 6.4 ± 4.7 years (1 month-18 years) (median value 5.4 years). Of the cases, 2865 (58.6%) were male. The sensitization of at least one allergen was 33.4% and the highest sensitization was with pollens (21.5%). Then, respectively, house dust mites (8.1%), animal epithelium (3.8%), mold (2.5%) sensitization were detected. Food allergen sensitization was found in 23.7% of 1165 patients who were tested with food allergens. Grass sensitization was the most common (%19.3) among pollen sensitizations. The frequency of allergen sensitization was 25.9% at < 2 years of age; 16.8% at 2-5 years of age; 39.6% at 5-12 years; 54.2% at > 12 years of age ($P < 0.001$). The most common allergy among 0-2 years was food (20.5%), among 2-5 years (8.6%) was pollen, 5-12 years (31.7%) was pollen and > 12 years (46%) was pollen sensitization. The frequency of eosinophilia was 59% in patients with atopy and 35.9% in patients without atopy ($P < 0.001$). Of the patients with atopy, 55.5% had a high IgE value, while this rate was 26.2% in patients without atopy ($P < 0.001$)

Conclusion: In our study, the most common sensitization in our region is pollen, the second is house dust sensitization. While food allergens were more prominent under 2 years of age, aeroallergen sensitivity was gradually increased as age increased

TP1497 | Transition of children with significant allergies and complex special needs- our experience

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Case Report:

Introduction: Living with an allergy can be a significant challenge for both parents and children. Added to the everyday challenges of living with allergies, any additional condition with complex learning needs, such as Autism and ADHD can make patients particularly vulnerable in areas such as communication, social interaction and self-care. The provision of transition into adult services for paediatric allergy patients is very varied and there is often no clear structure for transitioning patients. Arranging these transitional services for children with additional special needs can be even more demanding. There is a requirement for adapted transitional arrangements in this special group of patients. Aim: To illustrate through 2 cases an enhanced transition process from paediatric care to adult services, providing ongoing person-centred care to patients with allergies and complex learning needs.

Case Description: Both patients are over 16 and have confirmed the diagnosis of anaphylaxis to foods (shellfish and nuts), Autistic spectrum disorder and learning difficulties. Although they have an understanding of their allergies, due to their poor communication skills and learning difficulties, we have identified additional barriers in handing over their care to adult allergy services. We developed a unique personalised patient centred plan with reasonable adaptations after a capacity assessment. Engagement with clinic and investigations was improved using distraction, rewards and communication widget tools. Clinic visits were carefully designed to ensure consistency in the room and staff. The patients were seen by an adult allergy team within the paediatric setting. The adult and paediatric safeguarding teams were consulted.

Outcomes: The enhanced pathway resulted in reduced stress and anxiety during clinic appointments culminating in a successful transition to adult services. It also allowed for completion of education and investigations, including phlebotomy, without anxiety or distress for the patient.

Conclusion: It is possible to provide high-quality care to this unique and challenging patient group by recognising the additional barriers to treatment and making reasonable adjustments to their individualised care plans, which are structured to meet distinct needs (National Autistic Society, Equality Act 2010)

TP1498 | Prevalence of IgE sensitization to food and respiratory allergens in children

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Background: Allergy is becoming more common disease in the world. The profiles of sensitization in children determine the possible development of allergy in their future life. So the aim of this study was to investigate the epidemiology of children sensitization in West part of Russia.

Method: Children (n = 115; 6-12 years of age) random taken were studied. MeDALL-chip (176 allergen molecules) was used to assess of IgE-antibodies levels in serums of individuals. Sensitization was considered to be significant when the level of antibodies was ≥ 0.30 ISU for MeDALL.

Results: 25.2% of children were defined as sensitized to at least one of the allergenic molecules of the MeDALL chip. A one-allergen sensitization was found in 13.4% children, 6.1%, 3.5% and 2.6% children had sensitization to 2-3, to 4-7, and to ≥ 8 allergens, respectively. Most frequently, the sensitization was caused by respiratory allergens alone (14,% children) or in a combination with food allergens (7.8%); in 2.6% individuals only food allergens were responsible for the sensitization. Cat allergen (Fel d1) and birch allergen (Bet v1) were the essential provoke factors of allergy for 13.9% and 7.8% children respectively. IgE-antibodies to Fel d2 molecules were detected in 5.2% children. Also 4.35% of children had IgE to alder (Aln g1). Sensitization to dog (Can f1), house dust mites (Der f2, Der p2), timothy grass (Phl p1) and Alternaria alternata (Alt a1) were observed in 3.48% of children. But such well-known respiratory allergens like Amb a1 and Can f5 caused sensitization in only 2.56% of children. Important food allergens originating from egg or milk caused sensitization in < 2% of children. Only 1.74% of individuals were sensitized to milk (Bos d6, Bos d Lf), egg (Gal d3), peanut (Ara h9). We found 5.2% of patients with IgE-antibodies to Mal d1, but in all cases the high level of IgE to birch (Bet v1) was also observed. The sensitization to minor plant allergens was rare. IgE to Bet v2, Phl p4, Phl p5b, Phl p12 was detected in 1.74% children, and to Phl p7, Art v3 – only in 0.87% individuals.

Conclusion: Children of 6-12 years of age are more often sensitized by respiratory allergens having IgE-antibodies against 1 to 3 allergens. Cat and birch represent principal respiratory allergen sources. Sensitization to minor allergens occurs in ≤ 2% of the examined children. Sensitization to food allergens is less frequent, but often coinciding with cross-sensitization to respiratory allergens.

TP1499 | Evaluation of clinical symptoms and clinical course in pediatric patients with tree nut allergy

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Background: Tree nut (TN) allergy is an important health problem due to the fact that elimination is difficult in children, may cause severe reactions such as anaphylaxis and the frequency of resolution with age is low. We aimed to add information about the clinical characteristics and tolerance development of tree nut allergies in children.

Method: Clinical characteristics, laboratory findings and prognosis of patients who were followed up for TN allergy between 2010-2017 at University of Health Sciences, Ankara Child Health and Diseases Hematology Oncology Training and Research Hospital, Child Allergy Clinic were evaluated. Patients whose last control for the determination of the clinical course is more than 6 months were invited to the clinic; allergy work-up was repeated. Tolerance status was assessed by oral provocation test in patients with negative results.

Results: The mean age of the 128 patients (%73.4 male) included in the study was 2.5 (0.15-17.8) years. One hundred and nine patients (85.2%) had hazelnuts allergy, 60 (46.8%) had walnuts allergy, 47 (36.7%) had pistachio allergy, 37 (28.9%) had almonds allergy, 22 (17.2% had cashew allergy. Eighteen (33.3%) [16 (88.9%) hazelnut allergy, 2 (11.1%) walnut allergy] of the 54 patients with single TN allergy has improved. Of the 74 patients with more than one TN allergy, 21 (28.4%) hazelnuts allergy, 13 (17.6%) almonds allergy, 10 (13.5%) walnuts allergy, 5 (6.8%) pistachio allergy, 2 (2.7%) cashew nuts allergy has improved.

Conclusion: In our study, hazelnut and walnut allergy were the most common cause of TN allergies. In our patients, the rate of other food allergies associated with TN allergy was high. The recovery of patients with a single TN allergy (33.3%) was higher than the patients with multiple TN allergy(32.4%). Regular follow-up and evaluation of patients with TN allergy is very important.

TP1500 | The prevalence of systemic reactions and their sensitization profiles in children with pollen food syndrome

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Background: Little is known about the prevalence of systemic reactions (SR) and the importance of sensitization profiles in children

with pollen-food syndrome (PFS). The aim of this study was to evaluate the prevalence of SR associated with PFS and sensitization profiles in children.

Method: A total of 128 patients aged 5-17 with seasonal allergic rhinitis/rhino conjunctivitis (AR/ARC) were enrolled in this study. The questionnaire on rhinitis and food symptoms, skin prick testing with commercial aero- and food allergen extracts, total IgE and specific IgE (sp. IgE) to major pollen molecules PR-10 proteins (rBet v 1, rAra h 8, nGly m 4, rCor a 1, rMal d 1, rPru p 1), profilins (rBet v 2, rPhl p 12) and LTP (rPru p 3, nArt v 3, rCor a 8, rAra h 9, rJug r 3) using ImmunoCAP were performed. Statistical a multiple regression and univariate analysis were used.

Results: Of all AR/ARC patients clinical diagnosis of PFS was made in 48 (37.5%) children with median aged 9 y.o. Among included PFS (+) patients, 5 (3.9%) had a history of anaphylaxis and 19 (14.8%) of generalized urticaria with or without oral cavity reactions/symptoms. Nuts and peach were the most common food implicated in SR, which registered in 16 birch and 8 mix (birch and weed) allergic patients. All patients with SR had elevated specific IgE to both rBet v 1 and rCor a 1. Sensitization to rAra h 9, rCor a 8, r Pru p 3, nArt v 3 was prevalent (in 42.8%, 28.6%, 19.0%, 14.3% respectively) and had higher values among patients with SR. There were no patients with increased IgE to profilins. Sensitization to both rBet v 1 and nArt v 3 directly correlated with clinical symptoms of systemic reactions in PFS patients.

Conclusion: The prevalence of systemic reactions in children with PFS is low, with nuts and peach predominantly implicated. Specific IgE to rCor a1 and LTPs (rAra h 9, rCor a 8, rPru p 3, nArt v 3) in children with PFS seemed to be risk factor for development SR.

TP1501 | The natural history of egg allergy and factors associated with prognosis

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Background: Egg allergy is the second most common food allergy in children. Although most of the patients develop tolerance in early years of life, in some patients egg allergy may persist for longer time. The aim of this study is to investigate the tolerance processes and the clinical and laboratory factors associated with natural history of egg allergy.

Method: The study included patients, who were at least two years old, diagnosed with egg allergy and are followed for at least six months at our pediatric allergy clinic. Sociodemograpic features, symptoms, age at symptoms onset, age of diagnosis, clinical findings at diagnosis and during observation were recorded. Tolerance development status and tolerance development time were assessed

Results: A total of 173(69% male) patients were studied. The median age of symptoms onset was 4 month and the median age of egg allergy diagnosis was 7 month. Presenting symptoms were observed in 97.1% of the patients as skin symptoms, 2.9% gastrointestinal system, 1.2% respiratory system symptoms and 3.5% of the patients had anaphylaxis. Forty-five percent of the patients had another food allergy. The most commonly accompanying allergen was cow's milk(47.4%). Respectively, other food allergies were 8.7% legumes, 8.1% tree nuts and 6.4% wheat. Among the patients with egg allergy, 78.6% had mixed type hypersensitivity, 20.2% had IgE mediated hypersensitivity and 1.2%% had non-IgE mediated hypersensitivity reactions. Among the mixed type hypersensitivity patients, the most common symptom was atopic dermatitis(76.9%). At the end of a mean follow-up 23.5 ± 16.9 months, 36.4% of the patients developed tolerance by age 2 years, 78.6% by age 5 years. Totally 83.2% of the patients developed tolerance. Persistence was more common among, patients with anaphylaxis, accompanied by legumes and nuts allergies and patients with higher egg specific IgE levels, at admission .According to regression analysis high egg specific IgE value at admission was the factor associated with persistence (P = 0.012, OR:1.052, %95)

Conclusion: In our study, 105(60.7%) of 173 patients with egg allergy developed tolerance before 3 years of age. The presence of high specific IgE levels at the time of diagnosis were found to be related to persistence of egg allergy.

TP1502 | Bird-egg syndrome in pediatric age: Two cases report

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Background: Egg allergy is highly frequent in childhood, mainly due to egg white (EW) consumption. The principal allergens are ovalbumin, ovomucoid, ovotransferin, and lysozyme (contained in egg white). Egg yolk (EY) also contains proteins implied in allergic reactions such as alpha -livetin. This protein is also present in muscle tissue of poultry, being responsible for bird-egg-syndrome (BES), which is infrequent in children. Patients have respiratory and gastrointestinal symptoms with egg intake or with contact with birds.

Method: Children aged 1-14 years reporting egg allergy from January 2015 to December 2018, were analyzed. Demographic data, atopic personal and family history, skin prick test (SPT), prick-prick (PP) and specific IgE were included.

Results: 686 patients were analyzed. 684 were allergic to EW and 2 patients were diagnosed of bird-egg-syndrome.

The first patient was a 9 years boy with a positive background for atopy and allergic to nuts. His first egg reaction was with a fried egg, reporting oral allergy syndrome (OAS). Later he tolerated boiled and baked egg. After egg reaction he had also OAS with turkey and chicken meat. No respiratory symptoms were reported and he never had contact with any birds.

He had a positive SPT to EY and negative to EW, ovalbumin and ovomucoid. The PP to chicken was positive. Chicken specific IgE was 3.23 kUa/L, ovalbumin IgE < 0.35 kUa/L, ovomucoid IgE 0.75 kUa/L, EY IgE 7 kUa/L, EW IgE 0.9 kUa/L and alpha livetin IgE 2 kUa/L.

The second patient was a 4 years adopted girl from Ethiopia without atopy. She had vomits and OAS 30 minutes after eating omelet. Since then, she tolerated baked egg an afterwards she had a reaction while eating fried chicken. She reported vomits and abdominal ache. She never had neither respiratory symptoms nor contact with birds since she was adopted.

The SPT was positive to EY and negative to EW, ovalbumin and ovomucoid. PP was positive to raw and cooked chicken. EW IgE 3.53 kUa/L, Ovalbumin IgE 0.83 kUa/L, Ovomucoid IgE 0.43 kUa/L, EY 7.37 kUa/L, alpha livetin IgE 1.5 kUa/L.

Conclusion: BES is an infrequent entity in pediatric age that must be considered in patients reporting egg or chicken reactions. None of the patients had respiratory symptoms and had never had contact with birds. They had probably an intestinal sensitization, instead of a respiratory sensitization which is most frequent in adults. Both children tolerated cooked eggs and poultry.

TP1503 | Fecal calprotectin as a biomarker of IgE-mediated food allergy in children with atopic dermatitis

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Background: Fecal calprotectin (FCP) is a biomarker of intestinal inflammation. As intestinal inflammation plays an important role in the development of immune-mediated diseases, such as allergies, it is proposed that FCP could serve as a diagnostic biomarker of food allergy (FA) in children. The aim of this preliminary investigation was to compare FCP level in infants and children under 4 years of age suffering from atopic dermatitis (AD) with and without IgE-mediated food allergy (FA), with FCP level in healthy controls.

Method: In total, 23 infants and children (age, mean 13 months ± 12) newly diagnosed with AD were divided in two groups: G1, children with atopic AD with FA (N = 15), 2) G2, children with AD without FA (N = 8). Control group (G3) consisted of healthy children of the same age (N = 7). In G1 and G2, a complete blood count, total immunoglobulin (Ig) E, specific IgE to nutritive allergens, immunoglobulins, FCP and SCORAD score were assessed, while in G3 only FCP was assessed.

Results: The median FCP was 67 (IQR 187) μg/g in the 23 infants and children with AD and 74.1 (IQR 666.4) μg/g in the control group (P = 0.9024). There was no difference between G1 and G3 in FCP level (G1: median 70, IQR 413 μg/g vs G3: median 74.1, IQR 666.4 μg/g; P = 0.8878). There was no difference between G2 and G3 in FCP level (G2: median 31, IQR 73.5 μg/g vs G3: median 74.1, IQR 666.4 μg/g; P = 0.5628). The median FCP was significantly higher in G1 in comparison to G2 (G1: median 70, IQR 413 μg/g vs G2: median 31, IQR 73.5 μg/g; P = 0.0259). We have found a significant correlation between the FCP level and percentage of eosinophils (r = 0.6041, P = 0.0287), immunoglobulin (Ig) G level (r = −0.7281, P = 0.0073) and IgA level (r = −0.7250, P = 0.0076). There was no significant correlation between FCP level and the SCORAD score (r = *0.3657*, P = 01488). SCORAD score significantly correlated with white blood cells (r = −0.7275, P = 0.0048), IgG (r = −0.6590, P = 0.0197), IgA (r = −07263, P = 0.0075) and IgM (r = −0.6836, P = 0.0142).

Conclusion: Our preliminary results showed a significant difference in FCP level in patients with AD without FA in comparison to patients having both, AD and FA. However, these results should be confirmed on a larger number of subjects in order to assess the role of FCP as a biomarker of IgE-mediated FA in infants and children with AD and FA.

TP1504 | Serum vitamin D levels in food allergy patients are lower than those in healthy children

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Background: Many studies suggest that Vitamin D (VD) insufficiency contributes to allergen sensitization and allergic diseases, but those findings vary among populations. In the EAACI congress 2018, we reported that almost all pregnant women and a half of children have VD deficiency in Japan. The aims of this study were i) to evaluate VD levels in food allergy patients, ii) to assess the differences in VD levels between food allergens.

Method: Study subjects were children with cow's milk allergy (n = 109) or with hen's egg allergy (n = 75). All patients were diagnosed as food allergy based on the results of oral food challenge tests. Control subjects without food allergy were selected from a longitudinal birth cohort study (CHIBA study).

Serum VD levels were measured using liquid chromatography tandem mass spectrometry.

Written informed consents were obtained from subjects' parents.

Results: Median VD levels (ng/mL) in food allergy patients and control subjects were 15.9 and 21.0 (at 1 year of age), 16.7 and 21.2 (at 2 years of age), and 22.4 and 23.2 (at 5 years of age), respectively. VD levels in food allergy patients were significantly lower than those in control subjects ($P = 0.027$ for 1 year of age and $P = 0.006$ for 2 years of age). Subgroup analysis revealed that VD levels in milk allergy patients were significantly lower than those in control subjects, but VD levels in egg allergy patients were not.

Conclusion: VD levels in food allergy patients are lower than those in healthy children. There may be some difference in VD levels among allergic food. We need to search factors (c.f. dietary habit) which lead to those variations.

TP1505 | Eosinophilic gastroenteritis found by pica during oral immunotherapy: A case report

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Case report: Eosinophilic esophagitis has been reported as a complication of oral immunotherapy (OIT), but there are only a few reports of eosinophilic gastroenteritis (EGE) occurring after OIT. EGE causes eosinophil infiltration into the gastrointestinal (GI) tract and is characterized by various digestive symptoms.

We report the case of a 6-year-old boy with EGE. He was diagnosed as having immediate-type food allergies (egg, milk and wheat) by food-challenge tests at 1 year of age. OIT for each food was carried out, and the amounts of the offending foods were able to be gradually increased without causing any immediate-type allergy symptoms. However, the total IgE and specific IgE values were remarkably increased at the age of 4 years and 4 months. He first developed oral mucosa symptoms and vomiting at 4 years and 10 months of age, and they gradually worsened. Stopping eggs and milk alleviated the symptoms. Nevertheless, he still occasionally vomited. He started Pica eating disorder (sand and sponge) due to anemia from 5 years and 10 months of age and developed eosinophilia without diarrhea or bloody stool (haemoglobin 7.1 g/dL, ferritin 1.6 ng/mL, eosinophil 27.6%, albumin 3.6 g/dL, stool Hb negative). Upper and lower GI tract endoscopic examinations found no bleeding. The GI mucosa showed eosinophil infiltration of more than 40/high-power field in the stomach and duodenum, so he was diagnosed with EGE. No eosinophils were found in the esophageal mucosa. His GI symptoms and anemia improved on a multiple-food-elimination diet. Currently, we are identifying the causative foods by means of long-term food-challenge tests.

Patients undergoing OIT should be closely followed up for a long time, and those with GI symptoms should be evaluated by GI endoscopy.

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ASTHMA IN THE CLINIC

TP1506 | Severity of allergic asthma associated with sensitization to food allergens

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Background: Asthma is rarely a manifestation of isolated food allergy. Children with asthma and sensitized to at least one food allergen had a higher hospitalization rate and a systemic corticosteroid requirement. The objective of this study was to evaluate the sensitization to food allergens in patients with allergic asthma without a history of food allergy.

Method: Cross-sectional study of asthmatic patients with no history of food allergy in follow-up at the asthma outpatient clinic of a tertiary hospital. All patients had allergic asthma characterized by the presence of specific IgE to at least one aeroallergen. All of them were submitted to skin prick test to food allergen (milk, egg, fish, peanut, wheat, and shrimp) from ALC®.

Results: We included 49 patients with allergic asthma and negative history for food allergy. Of these, 23 patients (47%) had positive specific IgE for at least one food allergen: 17.4% for milk; 21.7% for egg; 60.9% for shrimp; 30.4% to peanuts, 26.1% to fish and 30.4% to wheat. When compared to the non-sensitized food allergen group, it was observed that those sensitized to at least one food allergen had a higher sensitization to cockroaches (30.4% *versus* 11.1%) and a higher frequency of uncontrolled asthma (52.2% *versus* 25.9%).

Conclusion: This study showed that half of the allergic asthma patients with no history of food allergy had sensitization to food allergens. The group sensitized to at least one food allergen had poorer control of asthma and a more frequent association of sensitization to cockroach and shrimp allergens.

TP1507 | Clinical and immunological evaluation of cat-allergic asthmatics living with or without a cat

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Background: In this observational study, we aimed to evaluate the impact of daily cat exposure in cat allergic asthmatics by spirometry and clinical symptom measures. In addition, immunological measures of T cell and basophil responses against the dominant cat allergen components Fel d 1, Fel d 4 and Fel d 7 were also performed.

Method: Twenty adults with history of cat-induced asthma and rhinitis, positive cat dander-specific serum IgE (>0.35kU/L) and Skin Prick Test (SPT) at screening were enrolled at a 1:1 ratio according to cat ownership. To compare the two groups, cat extract- and Fel d 1- specific basophil sensitivity test (BST), serum specific IgE, IgG4 and SPT were measured on Day 1 and Day 28; ambulatory spirometry and symptom measures were obtained daily. Fel d 1 and Fel d 4-reactive CD4 + T cells were tracked and profiled using a CD154 upregulation ex-vivo assay.

Results: Significantly higher cat allergen levels were detected in the homes of cat owners vs non-cat owners. Cat owners had higher symptom scores (nasal, ocular, respiratory), higher medication use and a trend toward lower FEV1 compared to those not living with cats. Significantly higher levels of cat dander specific-IgG4 were observed among cat owners, but no significant difference for cat-dander specific IgE or SPT. All subjects tested positive on BST to Fel d 1 and cat dander extract. Cat-ownership was associated with reduced basophil sensitivity to Fel d 1 (IC 50), but had positive BST to Fel d 4 and 7, as measured by CD203c and CD63. T cell response to Fel d 1 and Fel d 4 were differentially polarized, with Fel d1 responses strongly polarized toward Th2 responses. No significant correlation was observed between basophil reactivity and T cell responses against individual cat allergens.

Conclusion: Cat allergic subjects who live with a cat demonstrated reduced pulmonary function and greater clinical symptom severity, despite higher medication use and IgG4. BST demonstrated a significant immunological difference between cat allergics who are cat-owners vs non cat-owners. Cat ownership was associated with higher Th2 response against Fel d 1 but not to Fel d 4 suggesting no link between T cell and basophil responses.

TP1508 | Analysis of fungal allergen and aspergillus fumigatus component sensitization in patients with respiratory diseases in southern China

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Background: Fungal spores and hyphal fragments in air reportedly cause immunoglobulin E (IgE)-mediated respiratory allergic diseases.

	ABPA (n = 18)		AS (n = 30)	
	Positive rate n (%)	sIgE level (kU/L) median (interquartile)	Positive rate n (%)	sIgE level (kU/L), median (interquartile)
Asp f 1	16 (88.9)	7.93 (1.40-30.18)	22 (73.3)	1.21 (0.24-10.65)
Asp f 2	12 (66.7)	3.46 (0.08-9.10)	15 (50.0)	0.35 (0.03-3.00)
Asp f 3	12 (66.7)	0.83 (0.07-11.53)	18 (60.0)	1.03 (0.04-4.62)
Asp f 4	11 (61.1)	3.20 (0.10-17.65)	14 (46.7)	0.21 (0.02-12.93)
Asp f 6	12 (66.7)*	1.22 (0.07-5.70)†	8 (26.7)	0.03 (0.01-0.61)

However, there is a lack of detailed studies investigating the sensitisation caused by various mycotic allergens and *Aspergillus fumigatus* components. We analysed the prevalence of fungal allergens in patients in Southern China and discussed sensitization to seven fungal allergens in patients with respiratory allergic diseases. We also analysed roles of *Aspergillus* components in the differential diagnosis of ABPA and asthma.

Method: In total, 4033 patients with respiratory diseases were enrolled in this study to analyze the prevalence of aspergillus fumigatus. SIgE against to *Aspergillus fumigatus*, *Penicillium chrysogenum*, *Cladosporium herbarum*, *Mucor racemosus*, *Candida albicans*, *Alternaria alternata*, and *Helminthosporium halodes* were further tested. The role of *Aspergillus fumigatus* components in the differential diagnosis of ABPA and asthma was investigated.

Results: Among 4033 patients, 7.30% were positive for *Aspergillus fumigatus* allergen-sIgE, with an median sIgE level of 1.10 (0.54-3.79) kU/L. Notably, *Aspergillus fumigatus* accounted for 21.8% of all fungus-positive cases. The six fungi had high positivity rates in co-sensitization to *Aspergillus fumigatus* (84.6-100%). *Aspergillus fumigatus* was correlated with all other fungi (0.51-0.82,). The correlation between *Aspergillus fumigatus* and Asp f 2 was the strongest (r = 0.73). The positivity rate and sIgE level of Asp f 6 were significantly higher in patients with ABPA than in patients with asthma (P < 0.05, Table 1).

Conclusion: Overall, these findings showed that fungi had important sensitizing effects in patients with asthma and ABPA. Asp f 6 measurement may facilitate the differential diagnosis of ABPA and asthma.

TP1509 | Differences in clinical characteristics between aspergillus fumigatus sensitized asthmatics and allergic bronchopulmonary aspergillosis

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Background: *Aspergillus fumigatus* sensitized asthma patients (AFSA) are prone to develop into allergic bronchopulmonary aspergillosis (ABPA). This study aims to explore the characteristic of these patients and accurate diagnosis between diseases.

Method: The sIgE of *Aspergillus fumigatus* was detected by ImmunoCAP 1000 system in 17 patients with ABPA and 14 patients with AFSA. The sIgG of *Aspergillus fumigatus* was detected by *Aspergillus fumigatus* specific IgG ELISA kit (DRG). Clinical data such as pulmonary function and blood routine were collected.

Results: There was no significant difference in blood routine and induced sputum between ABPA and AFSA patients, but the levels of sIgG [2294.00 U/mL (1527.00, 14170.00) vs 972.60 U/mL (650.90, 1792.00)], sIgE [8.77 kU/L (1.64, 16.85) vs 1.04 kU/L (0.70, 2.05)] in ABPA patients were significantly higher than those in AFSA patients (P < 0.05). *Aspergillus fumigatus* sIgG was strongly correlated with *Aspergillus fumigatus* sIgE (r_s = 0.797, P < 0.001) in ABPA patients, but weak in AFSA patients. When combined with *Aspergillus fumigatus* sIgE (>1.00 kU/L) and *Aspergillus fumigatus* sIgG (>1000.00 U/mL) for the differential diagnosis of ABPA and AFSA, the sensitivity and specificity reached 82.3% and 78.6%

Conclusion: ABPA patients have higher levels of sIgE and sIgG of *Aspergillus fumigatus* than AFSA patients. Combination of sIgE and sIgG of *Aspergillus fumigatus* to diagnosis ABPA and AFSA patients is important.

TP1511 | Immunological markers of secondary immune deficiency in patients with bronchial asthma

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Background: Aim: To study the clinical and immunological features of the phenotype of bronchial asthma with syndrome secondary immune deficiency.

Method: The analysis of observations 105 patients with bronchial asthma (BA), which is 66.6% (70 patients) showed clinical markers of secondary immune deficiency. As a control, were examined patients with bronchial asthma without secondary immunodeficiency (35 patients).

Results: Found that patients suffering from bronchial asthma with secondary immune deficiency, there is inhibition of cellular (CD_3+

52.8 ± 2.2%, CD_3+CD_4+ 32.7 ± 1.8% of control, respectively: CD_3+ 72.6 ± 3.9%, CD_3+CD_4+ 40.5 ± 2.8%) and phagocytic (factor stimulation 1.48 ± 0.21; of control 1.97 ± 0.28) links on the background of activation of the humoral (CD_3-CD19 + 13.78 ± 1.39%; IgG of 13.28 ± 3.67 g/L; Total IgE 287.4 ± 63.2 ME/mL, control: CD_3-CD19 + 8.32 ± 0.76%; IgG 11.60 ± 3.25 g/L; Total IgE 147.2 ± 12.4 ME/mL; circulating immune complexes 129.2 ± 21.7 ed. control: 59.20 ± 10.47 ed.) immune system. Changes in immune status are recorded on the clinical course of the disease.

Conclusion: In patients with bronchial asthma with a concomitant syndrome secondary immune deficiency are heterogeneous disorders of the immune system, leading to clinical manifestations of secondary immune deficiency (frequent acute respiratory viral infections, exacerbation of herpetic infection associated with inflammatory diseases; the relationship of asthma exacerbations of chronic inflammatory diseases), making it difficult for bronchial asthma, contributes to chronic foci of infection, refractoriness to traditional treatment methods.

TP1512 | Predictors of chronic lung disease in patients with common variable immunodeficiency

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Background: Pulmonary complications occurred in about 30% of the patients with common variable immunodeficiency (CVID), and the chronicity of pulmonary infectious diseases determines a worse prognosis. Objective: To associate tomographic pulmonary alterations, history of the disease and results of laboratory tests of patients with CVID.

Method: A cross-sectional study, including 17 patients with CVID who underwent chest X-ray, spirometry, levels of immunoglobulins IgA, IgM, IgG, IgE and CD3, CD4, CD8 and CD56 lymphocytes at baseline.

Results: The mean age was 36.8 ± 10.53 years old, 67% female, age at onset of symptoms was 12.72 ± 7.69 years, and time between onset of symptoms and diagnosis was 14.22 ± 8.68 years. The mean IgG level at diagnosis was 133.77 ± 127.20 mg / dl and CD4 + T lymphocytes 585.85 ± 217.78 / mm^3. 67% had clinic pulmonary infection before diagnosis. 47% out of 70.5% of the patients with chronic pulmonary alterations, had bronchiectasis (BC) .40% also had chronic sinusopathy. Patients with bronchiectasis presented a shorter duration of disease (mean 11.38 ± 5.55 years), compared to patients without BC (17.44 ± 10.41 years), with no significant difference (P = 0.15). We also observed that patients with BC had started later (14.63 ± 6.84 years), (P = 0.18). Half of the patients had normal spirometry. The mean values for TCD4 and TCD8 were higher in the group without BC, 661.86 ± 252.00 and 1172.43 ± 452.39 / mm^3, compared to the group with BC, which was 509.86 ± 159.79 and 743.14 ± 626.31. There was no difference regarding the inversion of the ratio CD4 / CD8.

Conclusion: Pulmonary complications of CVID seem to be associated with earlier diagnosis and later onset, that means physicians are more worried with severe symptoms and with children. The higher CD4 levels at diagnosis appear to protect against the evolution of chronic pulmonary disease .

TP1513 | Periostin in serum and nasal material from patients with severe asthma of different age

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Background: The bronchial wall remodeling process is an important for the future lung function loss and patient's bronchial asthma (BA) progression. We evaluate the concentration of remodeling marker periostin and its correlation to FEV1, asthma duration and hospital admissions in severe asthmatics of three age groups.

Method: We included 28 children (aged 6-11 years, mean 9.2) (22 boys), 31 teenagers (aged 14-17 years, mean 16.7) (19 boys) and 29 young adults (aged 21-40 years, mean 33.4) (13 men) with asthma treated 4/5 GINA steps for previous year. Date of BA diagnosis, number of inpatient exacerbations and periostin level in serum and nasal wall brush biopsy material was determined. Data presented as M±σ or Me [Q25; Q75]. Mann-Whitney test used for comparison; correlations assayed with Pearson test. Differences assumed significant with $P < 0.05$.

Results: We receive significant difference in serum periostin level between adolescents (43.53 ± 2.97 ng/mL) and both children (34.04 ± 5.17 ng/mL) (P = 0.032) and adults (31.62 ± 4.35 ng/mL) (P = 0.029). Nasal material periostin concentration were lowest in children (3.18 ± 1.42 ng/mL) and significantly higher in adolescents (8.96 ± 2.29 ng/mL) (P = 0.0001) and adults (7.26 ± 3.08 ng/mL) (P = 0.008). We observe strong positive correlation between nasal, but not serum periostin and asthma duration (r = 0.71). Also both serum and nasal periostin levels were highest in subgroup of children with ≥ 2 last year BA exacerbations. FEV1 in adolescents and adults demonstrate strong negative correlation with nasal periostin (r = −0.84).

Conclusion: In patients with BA periostin can be measured not only in serum. Nasal periostin data are more efficient in lung function prognosis and future exacerbation risk assessment.

TP1514 | Type 2 inflammation in severe persistent asthma under subtropical climate conditions

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Background: The term endotype was recently proposed as a conceptual framework to guide new thinking about the molecular heterogeneity of asthma. The aim of this study is to describe the endotype

of 'TH2-high' severe asthma -characterized by increased levels of type 2 inflammation in the airways- in a geographical area with a high perennial house dust mite (HDM) exposure.

Method: Observational, retrospective, non-interventional study (CICSA Study, funded by AstraZeneca). Patients ≥ 12 years of age who has been diagnosed at our Institution with persistent severe uncontrolled asthma in accordance with the GINA guidelines in the last 6 months. Measured variables were: demographic information, asthma symptoms and medication use, medical history, and health care utilization (asthma exacerbations) and physiologic testing of lung function. Atopy status was assessed by skin prick testing (SPT) and/or measurement of serum total IgE to common airborne allergens and blood eosinophils.

Results: Twenty-four selected subjects (18 females, 14 to 68 y.o.) showed a mean rate of asthma exacerbations of 1.95/year, with a mean FEV1 of 75%, a total IgE (UI/mL) ranging from 41.3 to 1650.0, sIgE (kU/L) to *D. pteronyssinus* from 0.5 to > 100, a markedly positive SPT to local (*D. pteronyssinus*, *D. farinae and/or Blomia tropicalis*) mites (95.85%) and mean absolute blood eosinophils of 599.08 cells per μL. Nineteen out of the 24 patients were on biologic therapy at the time of data collection.

Conclusion: In the selected subset of patients with type 2 inflammation severe persistent asthma, besides the systemic eosinophilia, a remarkable specific IgE driven immediate response to relevant mite allergens was confirmed. The pathobiologic mechanisms of aeroallergens in the TH2-high severe asthma endotype are yet to be elucidated.

TP1515 | Vitamin D does not affect asthma development in real practice in Korean, one of temperate zones

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Background: Vitamin D deficiency has been shown to have an important role in immune responses. Recently vitamin D deficiency was found in allergic diseases. However, the role of vitamin D in allergic diseases is still controversy, especially in real practice. The serum vitamin D of Korean adults are lower than that of adults in western countries. Thus we studied the relation between asthma and serum vitamin D in real practice in Korea. Thus we studied the effect of serum vitamin D on the development of asthma in patients with chronic low respiratory symptoms in Korea

Method: To investigate whether the occurrence of asthma is related to serum vitamin D levels of Korean adults with chronic lower respiratory symptoms in one university hospital in Korea. A total of 348 patients with chronic lower respiratory symptoms were included in this study. We measured bronchodilator responses, methacholine bronchial provocations, skin prick tests for approximately 45 allergens and a specific IgE test in all patients.

Results: The mean age of study subjects (348) was 52.5 + 17.3 yr. Ninety five patients were diagnosed with asthma and their mean age was 52.1 + 19.2 yr, which was not different from that of non-asthmatics (52.7 + 16.5 yr n = 253). Patients with atopy were 220 and their mean age was 48.6 + 17.0 yr which was not different from that of non-atopic patients (58.7 + 15.5 yr, n = 128). The serum vitamin D level of asthmatics (16.04 + 7.27 mg, n = 95) was not significantly different from that of non-asthmatics (17.10 + 8.71 mg, n = 253, $P > 0.05$.) The serum vitamin D level of atopic patients (17.00 + 8.48 mg, n = 220) was not significantly different from that of non-atopic patients (16.56 + 8.19 mg, n = 128, $P > 0.05$). The serum vitamin D level of atopic asthmatics (16.10 + 7.27 mg, n = 67) was not significantly different from that of non-atopic asthmatics (16.14 + 8.73 mg, n = 28, $P > 0.05$.), either

Conclusion: The level of vitamin D of asthmatics does not differ from that of patients with other chronic low respiratory symptoms in real practice in a university hospital in Korea. The levels of vitamin D of patients with chronic low respiratory symptoms do not differ according to atopy. Thus, Vitamin D might not affect atopy as well as asthma development in real practice in temperate zones

TP1516 | Risk factors for reduced lung function after first wheezing episode: 7-year follow-up

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Background: Rhinovirus induced wheezing is commonly detected as a risk factor for later asthma. In school-age, deficit lung function indicates persistent asthma, and affection seems to maintain in adulthood. The aim of the study was to study risk factors for reduced lung function at school-age among children who had suffered their first wheezing at age 3-23 months.

Method: The study included first-time wheezing children aged 3-23 months from Vinku (n = 131; recruitment 2000-2002) and Vinku2 studies (n = 124; recruitment 2007-2009); both carried out in Turku University Hospital. Of these, 65 (25.5%) children completed the 7-year follow-up visit including spirometry and bronchodilation test using 0.4 mg of inhaled salbutamol. Asthma control medication was not allowed 4 weeks prior to spirometry. At study entry, patients were examined and followed carefully at ward by a study physician, parents were interviewed and they filled standard health questionnaire, comprehensive virus diagnostics was performed and allergy status was evaluated.

Results: At study entry, the median age of children was 11.6 months, 46 (70.8%) were males, 11 (16.9%) has eczema and 9 (13.8%) were sensitized. Patients having more severe clinical symptoms (cough and rhinitis, fever, or high C-reactive protein level), or use of antibiotic treatment in the time of the first wheezing episode had worse lung function in school-age ($P < 0.05$), either decreased forced vital capacity in 1 second or response to bronchodilator. Also, parental asthma was related to reduced lung function in school-age ($P < 0.05$).

Prednisolone treatment given in the time of the first wheezing episode, atopic sensitization, presence of eczema, eosinophil count, or rhinovirus infection were not associated with lung function.

Conclusion: This study shows that when discussing the risk factors for decreased pulmonary function after virus induced wheezing episode, we should focus to the hereditary risk factors and also clinical markers of the severity of wheezing episode.

TP1518 | Lost in the transition from paediatric to adult care? Experiences of young adults with severe asthma

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Background: The development of asthma is a dynamic process with substantial disease turnover from child- to adulthood. Certain forms of asthma may persist; severe asthma is more likely to, while mild asthma often goes into remission. Hence, healthcare providers have a major task in identifying adolescents who are in need of further care in order to avoid disease progression in adulthood. A transition into adult care is performed when adolescents are around 18 years old. However, the transition is often haphazard, and lack of clinical attention and of tools to assess readiness for transition are examples of common barriers to a transition from paediatric to adult care.

Studies of how young adults with asthma experience the transition from paediatric to adult care are sparse. Most qualitative studies to date have focused on the parent-child transition, i.e., the transfer of responsibility. The aim of this qualitative study was to describe how young adults with severe asthma experience the transition from paediatric to adult care.

Method: Participants with severe asthma in young adulthood were recruited from the ongoing Swedish population-based BAMSE cohort. Data were obtained through individual semi-structured interviews (n = 16, mean age 23.4 years), and the transcribed data were analysed with systematic text condensation.

Results: Five categories emerged based on the participants' experiences: 1) "I have to take responsibility": had to take more responsibility after the transition. 2) "Being involved": needed to be involved, not just their parents. 3) "Feeling left out": information about the transition had been missing. 4) "Lack of continuity and regularity": fewer follow-ups compared with earlier or none at all. 5) "Asthma is not taken seriously": asthma was underestimated both by healthcare providers and in society.

Conclusion: The risk of being lost to follow-up in the transition process was apparent, especially if moved from a paediatric asthma/allergy clinic to primary care. Therefore, healthcare providers need to increase their awareness of the difficulties that young adults with severe asthma face in the transition process. It is suggested that healthcare providers together with each patient prepare, plan, and communicate in the transition process for continued care.

TP1519 | Influence of the severity of asthma and disease control on the placentofetal blood flow

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Background: Hemodynamic processes in the mother-placenta-fetus system in pregnant women with asthma cannot be considered sufficiently studied. Existing data about the influence of disease severity and its controllability on the placentofetal blood flow are few and contradictory. The goal of our survey was to study hemodynamics in the uterine, umbilical and cerebral arteries of the fetus with the usage of Doppler ultrasound in patients with asthma of varying severity who received different types of therapy.

Method: Within the survey 72 pregnant women at 34 weeks of gestation suffering from asthma (5 – severe persistent, 17 – moderate persistent, 22 – mild persistent, 28 – mild intermittent) and 64 women without lung pathology (control) were examined with Doppler ultrasound. Inhaled corticosteroids (ICS) were prescribed to 55 patients, but 17 refused to receive ICS, replacing it with SABA and other drugs. Systolic-to-diastolic ratio (S/D ratio) in the uterine arteries (UtA),umbilical artery (UmA) and the middle cerebral artery of the fetus (MCA) was evaluated.

Results: S/D ratio increase in UtA and MCA of the fetus was revealed in women with asthma but the differences with the control group were not significant. In moderate persistent asthma patients was registered reliably higher S/D ratio ($P < 0.05$) in UtA (2.51 ± 0.29) compared to mild persistent (1.91 ± 0.18) and control groups (1.95 ± 0.13). In patients who underwent asthma exacerbation in the first trimester of pregnancy, the average values of S/D ratio in UtA (2.69 ± 0.12) had significant differences with control group. When comparing patients with mild persistent asthma who received ICS and who refused to do that no significant differences as compared with control group were detected. There was a trend of increasing the pressure in MCA of the fetus in patients who did not receive ICS(5.37 ± 0.57). When comparing S/D ratio in group with moderate persistent asthma, among patients receiving and not receiving ICS, there were obtained reliable ($P < 0.05$) differences of S/D ratio in UtA (1.91 ± 0.15 and 2.82 ± 0.59) and MCA of the fetus (4.39 ± 0.43 and 5.98 ± 0.68).

Conclusion: Blood flow state in UtA is influenced by: exacerbation of asthma in the first trimester of pregnancy, severity of asthma, the absence of basic therapy. Increase of S/D ratio in MCA of the fetus is registered in the absence of basic therapy.

TP1521 | Fertility treatment among asthmatic women with live births – associated with perennial allergy?

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Background: Asthma has been linked with prolonged time to pregnancy compared to healthy controls, and a higher requirement for fertility treatment. However, our knowledge of the impact of allergy on need of fertility treatment is limited.

Objective: In asthmatic women with life births, our aim was to explore a possible difference in need for fertility treatment in women with perennial allergy (animals, fungi and dust mites) compared to women with no allergy/seasonal allergy. The primary outcome of interest was fertility treatment.

Method: Women enrolled in Management of Asthma during Pregnancy (MAP) program at Hvidovre Hospital (HH), Denmark (since 2007) were divided into two groups, asthma with perennial allergy (cases) and asthma with seasonal/no allergy (controls). Previous analyses of the cohort have shown that female asthma is associated with higher proportions of fertility treatment compared to non-asthmatic controls, not least among women aged 35 years and older.

Results: Among asthmatic women with perennial allergy (n = 544, cases) and asthmatic women with seasonal/no allergy (n = 388, controls) 13.8% (n = 75) and 10.1% (n = 39), respectively, had had fertility treatment (OR 1.43, 95% CI 0.95-2.16, P = 0.087). Furthermore, this association remained statistically insignificant after adjusting for confounders, incl. BMI (OR 1.19, 95% CI 0.77-1.844, P = 0.43). In women ≥ 35 years, it was 28% (n = 44) and 20% (n = 19) of cases and controls, respectively, (OR 1.60, 95% CI 0.87-2.94, P = 0.132), and still insignificant after adjusting for confounders (OR 1.41, 95% CI 0.74-2.69, P < 0.293),

Conclusion: A trend towards an association between perennial allergy and need for fertility treatment compared to seasonal/no allergy, possibly statistical insignificant due to the relatively small sample size. The probable association between female asthma with perennial allergy and a reduction in fertility needs to be further explored.

TP1523 | An Online Survey Detected Specialty Specific Knowledge Gaps In The Maintenance Asthma Treatment Among Allergists, Chest Physicians, ENTs And Primary Care

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Background: April 2017 the Mexican Asthma Guidelines (GUIMA) were published. Before launch physicians' knowledge was explored related to key-issues of the guideline.

Method: A Surveymonkey® survey was sent out to board-certified physicians of 5 medical specialties treating asthma. Replies were analyzed per specialty against the GUIMA evidence-based recommendations.

Results: A total of 364 allergists (ALERG), 161 pulmonologists (PULM), 34 ENTs, 239 pediatricians (PED) and 62 general practitioners (GPs) replied to the survey. Spirometry is not routinely indicated when asthma is very probable by ALERG54%, PULM47%, ENT39%, PED65%, GP64%. A fictitious case proposed to the physicians with intermittent asthma was erroneously treated with ICS by ALERG9%, PULM11%, ENT28%, PED10%, GP11%. The mild persistent case received mistakenly ICS-LABA by ALERG25%, PULM26%, ENT33%, PED27%, GP23%. The 1st-line option for moderate persistent asthma was ICS(median dose) instead of ICS(low) + LABA for ALERG29%, PULM25%, ENT17%, PED27%, GP23% and in severe asthma maintenance treatment PULM20%, ALERG-ENT-PED-GP 22-34% failed to indicate LABA. Concerning the guidelines' recommendation to use one inhaler for maintenance&rescue in moderate-to-severe asthma, PULM45%, ALERG-ENT-PED-GP 56-80% (P < 0.00001), erroneously indicated ICS-salmeterol could be used, instead of ICS-formoterol. Oral b2 or theophylline are no longer recommended, but PULM37% and ALERG-ENT-PED-GP 42-62% (P < 0.01) still indicate their use. In severe asthma 61-73% of physicians consider adding LTRA to the treatment; only PULM38%, OTHERS12-25% consider adding tiotropium (P < 0.001) and 3-17% consider adding omalizumab, both guideline recommended add-ons. As for asthma in pregnancy, most surveyed are not aware budesonide is the 1st line option ICS.

Conclusion: An online survey could detect knowledge-gaps related to asthma treatment. Among all surveyed specialties there is ample room for improvement, including in the treatment of severe cases. Though in real-life asthma tends to be under-treated, surveyed physicians tended to over-treat the milder cases, thus clearly leaving

room for cost-savings. Caution should be taken in the promotion of the 'one-inhaler-for-all' approach, as many physicians don't understand the details of this treatment yet and erroneously opt for medication combinations not apt for this approach.

TP1524 | Inheritance patterns and the risk for asthma

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Background: Asthma is a major public health issue. Family history is an important risk factor for the development of asthma. There are no data on asthma inheritance in Durres, Albania with a population aprox. 500 thousand habitants, so the present study was undertaken to investigate the inheritance patterns of asthma and the effect of family history.

Method: A total of 100 children and 100 adults with clinically diagnosed asthma, along with 200 non asthmatic children and adults as controls were selected for the study. Information about the family history of each patients and controls was collected and analyzed pedigrees were also constructed.

Results: A history of asthma in any member of the family was observed in 52.1 per cent of cases and 4.2 per cent of controls ($P < 0.001$). A differential risk of developing asthma was noted in family history of asthma in different first and second degree relatives of children and adult patients.

Conclusion: Our results showed that family history of asthma is very important in the development of asthma in the offspring. Further studies are needed to be done to gather more data on this topic.

TP1525 | Evaluation of systemic production of nitric oxide and metalloproteinase-9 in algerian patients with allergic asthma during stable and exacerbation statue

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Background: Asthma is an heterogeneous disease defined as a chronic inflammatory disorder of the airways. The most common type of asthma is allergic asthma. It is characterized by a Th2 immune response. Moreover, there is considerable evidence suggesting that nitric oxide (NO) and Metalloproteinase 9 (MMP-9) plays a significant role in the physiopathology of allergic asthma. In this sense, the aim of our study was to evaluate the production of NO and MMP-9 in Algerian patients with allergic asthma.

Method: The NO and MMP-9 production was evaluated in plasma of patients with mild, moderate and severe allergic asthma and healthy subjects by the Griess modified method and gelatin Zymography respectively.

Results: Our results revealed a significant difference ($P < 0.0001$) in plasmatic NO levels of patients with allergic persistent mild, moderate, severe asthma compared to healthy subjects. In addition, no statistically significant differences were found between patients with stable and exacerbation statue for moderate and mild asthma. In contrary, for severe persistent asthma strong significant difference ($P < 0.001$) was observed between the stable and the exacerbation statue of patients.

In another hand, plasma levels of MMP-9 were not statistically different for the 3 categories of stable asthma compared with controls. However, in exacerbated asthma patients, this rate was statistically higher compared to controls ($P < 0.001$) for mild, and ($P < 0.01$) for severe allergic asthma.

Conclusion: Our data confirm the implication of NO in the pathogenesis of allergic asthma. Moreover, the MMP-9 appears to be linked with an exacerbated statue of allergic asthma and not with a stable statue.

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BRONCHITIS, EARLY WHEEZE AND MOLECULAR ALLERGY

TP1526 | The perinatal risk factors of acute bronchiolitis before one years old

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Background: Bronchiolitis is one of the leading causes for infant hospitalization and is associated with lower respiratory tract infections, which caused by virus. We evaluated effectiveness of breastfeeding and other perinatal factors affecting occurrence of hospitalization for bronchiolitis.

Method: In a prospective case-control cohort study, 150 infants with age no elder than 1 year old were enrolled in 2 medical centers from southern Taiwan. Questionnaires were distributed and by medical professionals. Children were grouped as "exclusive breastfeeding" and "mixed and exclusive formula milk feeding". The risk of hospitalization for bronchiolitis was evaluated by using univariate analysis. Logistic regression was applied to evaluate risks of hospitalization for bronchiolitis. Odds ratios (OR) with 95% confidence interval (95% CI) were calculated.

Results: Among enrolled infants 36.7% were diagnosed with acute bronchiolitis, and 15.3% were "exclusive breastfed". The risk of hospitalization for bronchiolitis was significantly lower in the "exclusive breastfeeding" group (OR: 0.222, 95% CI: 0.058-0.847). Also, history of respiratory viral infection during pregnancy was associated with significant increased risk of children's hospitalization for bronchiolitis (OR: 2.758, 95% CI: 1.095-6.948).

Conclusion: Exclusive breastfeeding and maternal URI reduced the risk of hospitalization for bronchiolitis in children within first year of life. Exclusive breastfeeding might be effective measure of prevention of lower respiratory tract infection in infant younger than 1 year old.

TP1527 | Three cases of pediatric diffuse panbronchiolitis: A disease difficult to distinguish from asthma

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Case Report:

Introduction: Sometimes, it is difficult to distinguish asthma from the other diseases with wheezing. Diffuse panbronchiolitis (DPB) is a chronic inflammatory lung disease frequently complicated with chronic sinusitis, causing respiratory distress. DPB in children are very rare and some cases are diagnosed as severe and difficult-to-treat asthma. We present three pediatric cases of DPB, each being treated as severe and difficult-to-treat asthma at another medical institution and were eventually diagnosed and treated as DPB.

Case Report: Case one was a 13 year-old Japanese boy; case two was a 12 year-old Japanese boy; and case there was a 10 year-old Japanese girl. Each of the cases were diagnosed and treated as severe and difficult-to-treat asthma without significant improvement. All cases demonstrated wheeze and course crackles in both lung fields and blood samples showing no remarkable signs of severe inflammation. Increase in cold agglutinin, decrease in forced vital capacity (FVC) and forced expiratory volume in the first second of expiration (FEV_1) on lung function tests, and bilateral diffuse centrilobular infiltrative shadows on high-resolution computer tomography (HRCT) were seen in all cases. Based upon clinical findings, radiological findings, past history and examinations, DPB was diagnosed and treatment was initiated with low dose macrolides. In case one, continuation of macrolides led to improvement of clinical status, quality of life, respiratory symptoms, lung function, and radiological findings. Remarkable improvement of lung function was seen after the discontinuation of inhaled corticosteroids. In case two, treatment with macrolides showed improvement of quality of life, and radiological findings eventually leading to suppression of further admissions. In case three, improvement of clinical conditions and quality of life was confirmed also.

Conclusion: We present three cases of pediatric DPB from a single facility. One case showed remarkable improvement after discontinuation of inhaled corticosteroids, hypothesizing that treatment of bronchial asthma might aggravate conditions for DPB patients. We emphasize the importance of further reports of DPB in children, considering that it would eventually lead to accurate diagnosis and treatment in the future.

TP1528 | Posttransplant bronchiolitis obliterans syndrome in children

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Background: Bronchiolitis obliterans syndrome (BOS) is a condition that leads to fibrotic occlusion and obliteration of small airways caused by immune-mediated damage. The diagnosis is based on

obstructive decline in lung function in the absence of other etiologies. In the respiratory function test, forced expiratory volume in 1 second (FEV1) is the most important marker of BOS intensity.

Method: In our study, we evaluated the demographic characteristics, spirometric, clinical and radiological data of 19 patients who developed BOS after the hematopoietic stem cell transplantation performed in Antalya and Göztepe MedicalPark Hospital and followed up in Akdeniz University Department of Pediatric Allergy-Immunology and Pediatric Pulmonology.

Results: Of the 19 patients, 12 (63%) were female and 7 (37%) were male. Primary diagnosis of the patients were thalassemia major (n = 6, 31.5%), acute lymphoblastic leukemia (n = 3, 15.7%), Fanconi anemia (n = 2, 10.5%), acute myelocytic leukemia (n = 2, 10.5%), T cell lymphoma (n = 1, 5.2%), juvenile myelomonocytic leukemia (n = 1, 5.2%), hemophagocytic lymphohistiocytosis (n = 1, 5.2%) and Omen syndrome (n = 1, 5.2%). The lowest FEV1 value of 6 patients who had SFT before HSCT was 92% and the highest FEV1 value was 119%. High resolution computed tomography of the patients revealed mosaic pattern, increase in peribronchial thickness, bronchiectasis and centrilobular nodular lesions. In the follow-up, 4 of the patients died.

Conclusion: Nowadays, the pathogenesis of BOS in children is not adequately clarified, resulting in the limitation of diagnostic and therapeutic recommendations. In order to prevent the development of BOS after HSCT and to stop the progression of the disease, there is a need for further studies in this area.

TP1529 | State of immunity in persistent asthma and bronchiolitis obliterans in children

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Background: To assess the state of immunity in persistent course of asthma and bronchiolitis obliterans in children

Method: 56 children with BO and 75- with BA of persistent flow up at the age of 16 years were under supervision. Monoclonal antibodies to differentiating antigens CD3, CD4, CD8, CD20 were used The concentration of pro-inflammatory interleukin IL-4 and anti-inflammatory cytokines Il-8, TNF-α was studied by an enzyme immunoassay.

Results: In BA, the level of CD3 and CD4 did not exceed the norm, either during exacerbation or remission. The content of CD8 significantly exceeded the normative index, both with exacerbation and during the remission of BA (56.9 and 53.6, respectively). In BO the percentage of CD8 was at the lower limit of the norm. The concentration of Il4 and Il8 during the exacerbation of BA was at the upper limit of the norm with a significant decrease in the remission phase, as well as the TNF-α level.

Conclusion: Thus, in the genesis of BA atopic mechanisms prevail, which are not highly dependent on the effect of cytokines. On contrary, the increase of concentration of Il-8 and the level of TNF-α. In a remission phase, the concentration of anti-inflammatory interleukins continued to exceed the normative indices, which indicates the persistence of inflammation and allows the use of these indicators as markers of the formation of chronic obstructive pulmonary pathology in older age.

TP1530 | Bronchial asthma in pre-school children: A population-based cross-sectional study in Altai region

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Background: It is necessary to study the prevalence and risk factors of bronchial asthma (BA) among pre-school children in order to develop the disease prevention strategy. Objective. Our aim was to study the prevalence, clinical and allergological features, and risk factors for BA in pre-school children living in urban settings of Altai Region.

Method: We conducted a cross-sectional study comprising 3205 children (age 3 to 6 years). At the screening stage children attending pre-school educational institutions in 5 cities of the Altai Region were enrolled. BA symptoms were determined using the ISAAC questionnaire. At the clinical stage BA was diagnosed based on criteria according to Global Initiative for Asthma (GINA) guideline.

Results: The prevalence of BA in children aged 3–6 years was 5.7%. 62.7% of them were previously diagnosed with BA. Most children – 59.4% had mild severity BA. Sensitization was detected in 70 percent of children with BA. Most often, there was established sensitization to house dust mites *Dermatophagoides pteronyssinus* (63.3%), birch pollen (46.6%), and cat fur (31.1%). The risk factors for BA were family history of allergies [odds ratio (OR) 3.2; 95% confidence interval (CI) 2.2–4.6], masculine (OR 2.2, 95% CI 1.5–2.3), preterm birth (OR 2.1, 95% CI 1.3–3.3), smoking parents (OR 1.6, 95% CI 1.2–2.9), (OR 1.8, 95% CI 1.2–2.8), contact with animals in the first year of life (OR 1.4, 95% CI 1.0–2.0).

Conclusion: The prevalence of BA was 5.7%. Most often detected sensitization to house dust mites, birch pollen and cat fur. The risk factors for BA are family history of allergies, masculine, preterm birth, passive smoking and contact with animals in the first year of life.

TP1531 | Serum periostin as a biomarker for the diagnosis of asthma in preschool children

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Background: Diagnosis of bronchial asthma in preschool children is rather difficult due to the inability to perform pulmonary function tests. In this situation, serum biomarkers, preferably non-invasive, may play an important role for the asthma diagnosis in preschool children.

Method: 56 children with asthma (BA) and 29 children without asthma aged 3-6 years were involved in the study. Bronchial asthma was diagnosed according to Global Initiative for Asthma (GINA) guideline criteria. Blood eosinophil counts, total immunoglobulin E (IgE) levels and serum periostin levels were assessed. Results were compared between BA and controls. Asthma diagnostic accuracies were calculated using receiver operating characteristics (ROC) curve analysis.

Results: Serum periostin levels in the BA group were 5.8 ± 3.1 ng/mL and were significantly higher than those in the control group (2.7 ± 1.2 ng/mL; $P < 0.001$). There were direct correlation between blood eosinophil counts and serum periostin levels ($r = 0.29$, $P = 0.0284$) and between IgE levels and serum periostin levels ($r = 0.66$, $P = 0.0001$). The area under the ROC curve (AUC) for periostin, eosinophil counts and IgE were 0.81, 0.75 and 0.86, respectively.

Conclusion: Serum periostin levels were significantly higher in children with asthma. ROC AUC values for periostin were equivalent to conventional biomarkers, including blood eosinophil counts and IgE levels, indicating the utility of serum periostin levels in diagnosing asthma in children.

TP1532 | Evaluation of hospitalization predictions of asthma scores in preschool children with acute asthma

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Background: Measurement of asthma severity in the hospital setting is important in clinical decision making. Although pulmonary function tests provide objective data on airways obstruction, these tests are not feasible or reliable in younger children. Therefore, several clinical severity scores for childhood asthma have been described. Pediatric asthma severity score (PASS), based on the clinical findings is a reliable and valid measure of asthma severity in children and it shows both discriminative and responsive properties. Clinical asthma score (CAS) is easy to apply and may be used in clinical decision making or as a valid outcome measure for therapeutic trials in children between 1 and 5 years of age hospitalized because of asthma. The aim of this study was to evaluate the predictions of hospitalization of two asthma scoring systems in preschool children presenting with asthma attack.

Method: Seventy patients aged 2 to 6 years with recurrent wheezing (at least two times) who were admitted to the Pediatric Emergency Department with an asthma attack between January 2016 and April 2016 were included in the study. The scoring forms of the patients (at the time of admission and at the end of the treatment) were filled by a pediatrician (NC). The patient group was compared with those who had 3 or more attacks in the last 1 year and those with less than 3 attacks.

Results: The scores of the patients who had 3 or more attacks in the last 1 year were found to be significantly higher than those with less than 3 episodes in the last 1 year ($P = 0.010$ for CAS and 0.019 for PASS) (Table 1). The application scores of the patients who received systemic steroid treatment at the attack were significantly higher than those who were not given systemic steroids ($P = 0.006$ for CAS and $P = 0.003$ for PASS). In the prediction of steroid administration, CAS was found to have a sensitivity of 73.7% in cut-off 5.5 and PASS in cut-off 5.5 with 52.6% sensitivity. In predicting the continuation of follow-up therapy, PASS was found to have 95% sensitivity at cut-off 3.5 and CAS at cut-off 5.5 with a sensitivity of 82.5%.

Conclusion: It was determined that scoring systems could be used to predict systemic steroid treatment and hospitalization in pre-school children with acute asthma.

TP1534 | Factors related to wheezing in toddlers in a primary health care center of a tropical city in Mexico

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Background: The "International Study of Wheezing in Infants (EISL)", is a cross-sectional, population based study, partially based on ISAAC. "(Http // www.isaac.auckland.ac.nz). It uses a validated questionnaire focussing on wheezing during the first year of life and risk/protective factors.

Method: We applied the EISL questionnaire regarding events that occurred during the first 12 months of the child's life. *Population:* 1001 mothers coming in for their child's check-up or 12-months' vaccination visit in a primary health care clinic at the outskirts of Villahermosa, a tropical city in the south of Mexico. *Evaluated factors*: Child factors: sex, caesarean section, breastfeeding, daycare attendance, common cold < 3 mo of life, complete vaccination schedule. Home factors: having airco, a bathroom, an indoor kitchen, carpet, other siblings, >6 persons, pollution, pets at birth, pets now. Mother's

Results				
Multivariate analysis	Wheezing children (%)	Healthy (%) (N = 390)	OR	95% CI
ATOPIC	(N = 256)			
Smoking during pregnancy	6.3	0.5	11.39	2.36-54.99
Common cold < 3 mo of life	62.1	33.6	3.72	2.59-5.36
Cooking indoors	62.1	33.6	3.72	1.27-4.54
Mold	38.7	14.6	3.48	2.28-5.30
Pets actually	40.2	26.2	1.69	1.09-2.62
NON-ATOPIC	(N = 57)			
Cesarean section	29.8	48.5	0.44	0.23-0.82
Common cold < 3mo of life	56.1	33.6	2.68	1.46-4.91
Siblings (>1)	100	40.3	0.33	0.18-0.61
Breastfeeding > 3m	50.9	65.6	0.50	0.28-0.91
Pets at birth	50.9	33.1	2.03	1.11-3.70

factors: Smoking during pregnancy, level of education, employment and cell phone. Data analysis was dual: 1) descriptively, for data related to the wheezing episodes. 2) case-control, with as cases 2a. atopic or 2b. non-atopic kids who wheezed versus healthy controls (non-atopic, non-wheezers). Odds ratios (OR) and confidence intervals (CI) were calculated with univariant and multivariant analyses for factors possibly linked to wheeze.

Results: Results: 999 questionnaires fulfilled inclusion criteria. Any wheeze: 31.3%, recurrent wheeze (3 or more episodes): 12.1%. See table for OR and 95% confidence intervals (CI) linked to atopic and non-atopic wheeze. Breastfeeding was almost protective in atopic children.

Conclusion: Atopic and non-atopic wheeze have partially the same risk or protective factors, but in some they differ.

TP1535 | Risk factors for asthma outcomes of wheezing in early life

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Background: Wheezing in children, especially in young children was increasing in China, but which child will continue and develop into asthma is unknown, and no data in this field in China are available. A prospective cohort of young children with wheezing was established to observe the characteristics and outcomes of childhood wheezing, and to explore the risk factors that may influence outcomes of wheezing in early life.

Method: Children under 6 years with wheezing episode in early childhood were seductively enrolled, and the diagnosis of asthma was made after a one year follow-up. Baseline data were analyzed separately as diagnosed and undiagnosed asthma, statistically significant factors were selected to enter the multivariate Logistic regression model.

Results: 107 children (male 62.6%, median age, 1.5 years, range, 0.3-5.8 years) were selected for analysis, and 48 (44.9%) of them were asthmatic children. Logistic multivariate regression analysis showed that blood eosinophils elevated at the onset of wheezing, rhinovirus positive in viral pathogens detection, milk sIgE positive in serum allergen testing were the risk factors of early childhood wheezing progress to asthma after one year. Age was a protective factor for early wheezy in young children.

Conclusion: Elevated blood eosinophil, rhinovirus infection, and elevated level of milk sIgE at the onset of early wheezing in young children were risk factors for the progression of wheezing into asthma in the next year. Increasing age was a protective factor for asthma outcomes of early wheezing.

TP1537 | Orally administered immunostimulant as a prevention of asthma exacerbation and wheezing in children - a systematic review

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Background: For more than 40 years, orally delivered nonspecific, bacterial-derived preparations (bacterial lysates, BL), have been used in Europe for prevention of recurrent respiratory tract infections. Their immunomodulatory has been demonstrated in various models in vitro, in animal studies and clinical trials. Recent data indicate that these immunoregulatory properties may also contribute to reduction of wheezing and asthma in children.

Method: PubMed, EMBASE and Cochrane Rev databases were searched (until August 2018). Included studies assess the efficacy of treatment with BL in improving asthma severity and preventing wheezing episodes in children. A standardized protocol was used for data extraction. Resulting data were analyzed and discussed by two independent groups of reviewers. Systematic review was created on the basis of PRISMA statement and guidelines from the Cochrane Collaboration.

Results: Of the initial 893 findings, 21 studies met the inclusion criteria. After full-text screening and data extraction, 7 trials were included in the review. 5 articles evaluating BL influence on asthma and 3 studies concerning wheezing were analyzed. A statistically significant decrease in the mean number of asthma exacerbation as well as wheezing episodes in the intervention group comparing to controls was noted in 5 and 2 studies respectively. Reduced cumulative duration of wheezing attacks was observed in 2 studies. Although, the quality of identified studies was relatively low due to methodological concerns, and analyzed trials exhibit great heterogeneity of measured outcomes, none of them demonstrate the ineffectiveness of BL.

Conclusion: Orally administrated BL display a promising activity in prevention of wheezing and asthma in children. Further well-designed trials with various bacterial lysates and targeting wheezy children are needed in the future. Studies that employ a longer follow-up period and immunological biomarkers are also needed. A systematic approach in further long-term studies is vital in order to establish a firm link between administering BL and alleviating asthma or wheezing.

TP1538 | Strong association of serum EDN and sensitization status detected by an allergen microarray, ImmunoCAP ISAC, in preschool children with recurrent wheeze

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Background: Wheezing in preschool children is a common symptom, but prediction of asthma in these children is difficult because conventional tests for asthma such as spirometry and exhaled nitric oxide measurement are difficult to perform at this age. Serum levels of eosinophil-derived neurotoxin (EDN) reflects eosinophil activation and multiple sensitization is reported to be a risk for developing asthma.

Method: Serum samples were measured for EDN and specific IgE (sIgE) in children aged 1 to 6 years with recurrent wheeze who participated in a clinical trial (BIOTOPE study; Allergy Asthma Immunol Res 2018;10:686-97) and in volunteering age-matched children (healthy controls) without history of wheezing. EDN measurements were done by an ImmunoCAP based immunoassay and sIgE to multiple allergen components by an allergen microarray, ImmunoCAP ISAC 112.

Results: A total of 100 samples at active wheezing from the recurrent wheeze group and 96 samples at healthy state from the healthy volunteers were analyzed. Serum EDN levels in the wheeze group were significantly higher than in healthy controls. Wheezing children were sensitized to a significantly wider range of components and had higher levels of sIgE than their healthy counterparts had. Prevalence of strong sensitization (ISAC ≥ 15 ISU-E) was significantly higher in those with high levels of EDN in both groups. The sensitization patterns were similar in both groups with house dust mite components being most common but with higher levels of sIgE in the wheeze group.

Conclusion: High levels of serum EDN are associated with recurrent wheeze and multiple/strong allergen sensitization in young children and may be a useful biomarker in predicting asthma.

TP1539 | Physicians' perspective on preschool wheeze – an international survey (2nd stage)

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Background: Lower respiratory tract diseases accompanied by wheeze are very common, occurring in around 30% of all children under the age of 6. This survey was initiated by the EAACI Task Force on Clinical Practice Recommendation for Preschool Wheeze to recognize unmet needs in management of wheezy preschoolers and to project the content of the EAACI recommendations.

Method: Informed by the comments of physicians in a preliminary survey, organised in November and December 2017, the final survey was prepared in May 2018 and distributed to EAACI Paediatric and Asthma section members (n = 2132). The survey consisted of two parts: general information about the participants and specific clinical questions. The second round of this survey was distributed via a national medical social network in Poland and was viewed by 1324 unique users.

Results: In total, 730 participants from 55 nations completed the survey. Most responders - 266 (36.4%) - cited the lack of diagnostic tools as the most pressing problem with the diagnosis of preschool wheeze or asthma in pre-schoolers. The most relevant diagnostic option in preschool wheezers, according to 370 (50.7%) of the responders, was response to treatment. A vast majority, 557 (76.3%) of the responders agreed that recurrent wheezers required a different approach in comparison to patients with a single episode of wheeze, with 341 (46.7%) choosing allergy tests as the most appropriate option. When asked to specify their problems or doubts in the management of preschool wheezers, the responders mainly selected bad compliance with 268 (36.7%) of responders. A large percentage, 312

(42.7%), of the responders stated that it was very important (5/5) to set the clinical practice guidelines for preschool wheeze.

Conclusion: The survey presented here is the first step taken by the EAACI Task Force in order to establish new, comprehensive official EAACI guidelines on preschool wheeze. This is the first survey exploring the challenges that the diagnosis and management of preschool wheeze pose for physicians. The survey reveals an unmet clinical need for guidelines in management of preschool wheezers for general practitioners, family physicians, paediatricians and allergy specialists.

TP1540 | The effect of breastfeeding on the risk of asthma at school age

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Background: Breastfeeding has been suggested to be protective against pediatric asthma, possibly resulting from modulation of the infant gut microbiota and its impact on the development of the immune system. The aim of this study was to investigate the effect of breastfeeding on asthma in schoolchildren in the Republic of Macedonia as a developing country with a high prevalence of breastfeeding and a low prevalence of asthma.

Method: Parental-reported data obtained through a survey of 2310 children aged 5-15 years from randomly selected schools in Skopje, Republic of Macedonia, was used. The association between duration of breastfeeding (less than 4 weeks/never, 4 weeks to 6 months, and more than 6 months) with current asthma-like symptoms and doctor-diagnosed asthma was investigated by multiple logistic regression after adjustment for confounding factors (sex, age, immunization status, daycare attendance, maternal prenatal smoking, prematurity).

Results: Current wheeze was documented in 6.5%, sleep-disturbing wheeze in 3.6%, exercise-induced wheeze in 1.7%, dry night cough apart from a cold/chest infection in 12.2%, congestion or phlegm in the chest apart from colds present for at least 3 months in a row in the past 12 months in 1.8%, and asthma in 2.3% of the children. Most children (69.3%) were breastfed for longer than 6 months. Breastfeeding 4 weeks to 6 months and more than 6 months, compared to breastfeeding less than 4 weeks/never, were negatively associated with current dry night cough (aOR: 0.63; 0.40-0.99; P = 0.046 and aOR: 0.71; 0.50-1.00; P = 0.050, respectively) and current congestion or phlegm in the chest (aOR: 0.22; 0.06-0.78; P = 0.019 and aOR: 0.46; 0.23-0.94; P = 0.034, respectively). A significant association between breastfeeding and other current asthma-like symptoms was not observed.

Conclusion: The findings support the effect of breastfeeding on the maturation of the child's immunity and health benefits against cough and congestion in the chest, as asthma-like symptoms, even at school age. Mothers should be encouraged to initiate breastfeeding and aim to breastfeed for more than six months.

TP1542 | Tree pollen in children with respiratory allergies in a single hospital in Busan

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Background: In Busan, Of the pollens, trees are the most important cause of allergies. In this study, children with asthma and rhinitis staying in Busan were investigated for tree allergen sensitization, the relationship between tree pollen counts and sensitization, and oral allergy syndrome.

Method: For 1 year, the pollen were measured in Busan by a rotorod sampler, dyed with Calberia's fuchisin dye, and pollen counts were calculated under a microscope. We conducted a study of children aged 6 to 15 with rhinitis and asthma at Busan St.Mary's Hospital in 2017, and also conducted an allergy test (ImmunoCap) and an ISSAC questionnaire and oral allergy syndrome survey.

Results: The total number of subjects was 57. The average age was 9.3 years old, seven of them were oral allergy syndrome (12.3%). In Busan, the tree pollen counts was in decreasing order: pine, alder, oak, juniper, beech, ginkgo, and birch. For sensitization by specific IgE (above 0.35kUA/L), birch and alder accounted for 35.1%, Japanese cedar 19.3%, juniper 17.5%, pine 10.5%, and Japanese cypress 8.2%. Pine had less sensitization rate to the number of pollen. Alder was the most representative trees in Busan, same fagales as oak and birch were highly correlated. Juniper is the most common tree pollen in pinales and had a high correlation with japanese cedar and cypress. Oral allergy syndrome was found in 3 peach, 3 peanut, 2 apple, 1 tomato, 1 kiwi and 1 sesame, which were associated with PR-10.

Conclusion: In children with asthma and allergic rhinitis in Busan, alder is the major tree pollen of fagales, and juniper is the major of pinales.

TP1543 | Patterns of molecular sensitization in children and adolescents in Dnipro region (Ukraine)

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Background: Molecular allergy diagnosis may contribute to a better diagnostic and selection patients for allergen-specific

immunotherapy. Patterns of sensitization may vary in different regions even within the same country.

Method: Medical history, anthropometry, clinical examination, total serum IgE and specific IgE to allergen extracts and allergen molecules (multiplex assay ALEX®) were evaluated in all patients.

Results: 94 children and adolescents with any history of allergic diseases were included in the study (60 men, mean age 8.7 ± 10.4 years old). Total serum IgE was 186.5 [76.00-529.00] kU\L

In accordance with serum specific IgE to allergen extracts the most common sensitization was to ragweed (76.6 %); Alternaria alternata (51.1 %); birch (46.8 %); cat (40.4 %); house dust mite (40.4%). More than 30 % of patients were sensitized to bermuda grass and chaff. More than 20% had sensitization to timothy grass, rye reed beech alder mary.

In accordance with test results for the specific IgE to allergen molecules the most frequent sensitization was detected for Amb a 1 (75.83 %); Fel d 1 (43.15 %); Alt a 1 (40.4 %); Bet v 2 (40.4 %). More than 30 % patients were sensitive to Pho d 2; Art v 1; Bet v 1; Ole e 2; Lol p 1; Der p 1. It should be noted that like in adults, high sensitization level for some molecules were detected in children and adolescent with normal total IgE.

Conclusion: Children and adolescents with history of allergic diseases in Dnipro region (Ukraine) more often sensitized to the ragweed, Alternaria alternate, birch, cat and house dust mite. The most common specific serum IgE were for Amb a 1, Fel d 1, Alt a 1, Bet v 2. The pattern of sensitization evaluated by serum IgE to extracts and molecular allergens are not entirely similar. Thus, identifying specific IgE to allergen molecules is useful tool for improve the diagnostic accuracy and detect the cross reactivity.

TUESDAY, 4 JUNE 2019
TPS 53
INFECTIONS: PATHOGENESIS AND TREATMENT

TP1544 | Dendrimeric peptide LTP exhibits potent antiviral properties against respiratory syncytial virus

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Background: Respiratory syncytial virus (RSV) is one of the most common viral pathogens. Natural peptides (defensins and cathelicidins) possessing antiviral properties are an important part of the innate immune system. However, their purification from natural sources is expensive. In this regard the main aim of this study was to design and synthesis of peptides with different structures and test their antiviral activity.

Method: 16 peptides with cationic properties were synthesized: SP-191, NC-777, NC-783, NC-810, NC-788, LO-7, NC-786, NC-771, NC-762, KO-1, NC-770, NC-785, IA-2, AS-543, NC-737, LTP. Toxicity was studied using MTT test. For antiviral activity assessment peptides were mixed with RSV strain A2 and incubated for 1 hour, after that the mixture titrated on MA-104 cells monolayer. The virus incubated with saline served as a control. After incubation for 3 days the cytopathic effect of the virus on cells was evaluated by light microscopy.

Results: The peptides NC-783 and NC-810 were most cytotoxic; IC_{50} were 0.04 ± 0.01 and 0.05 ± 0.01 mg/mL, respectively. LO-7, AS-543 and NC-785 peptides were less toxic; IC_{50} from 0.94 ± 0.15 to 2.72 ± 1.12 mg/mL. RSV incubation with 11 linear peptides: SP-191, NC-777, NC-783, NC-788, LO-7, NC-786, KO-1, NC-785, IA-2, AS-543 NC-737 significantly reduced virus titer in no less than 10 times. Dendrimeric peptide LTP at concentration 1 mg/mL maximally reduced the RSV titer in 100 times. Antiviral activity of LTP was dose dependent; the peptide reduced RSV titer in 50% at concentration 2 μg/mL. At the same time cytotoxic concentration LTP exceeded 2.5 mg/mL. Such potent antiviral activity is probably due to the substantial positive charge of this peptide which is provided by the presence of 8 arginine residues.

Conclusion: The dendrimeric peptide LPT exhibits potent antiviral activity against RSV and reduces the virus titer in 100 times that makes it a promising compound to develop drugs for the treatment of RSV infection including RSV induced asthma exacerbations.

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TP1545 | Effectiveness of MP-AzeFlu in patients with different allergic rhinitis phenotypes: A german, multicenter, prospective study

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Background: Patients with allergic rhinitis (AR) often have comorbidities such as eczema, chronic rhinosinusitis, otitis media, and asthma. Moreover, allergic comorbidities and IgE polysensitization are often linked with the persistence or severity of allergic diseases. This study evaluated the effectiveness of MP-AzeFlu (azelastine hydrochloride/fluticasone propionate nasal spray) among symptomatic patients with moderate-to-severe AR.

Method: This German, multicenter, prospective study was part of an international study and included patients for whom MP-AzeFlu

TABLE. VAS score change from baseline to last day of overall AR symptoms

ARP, mean (SD)	Day 1	Day 3	Day 7	Last day
ARP1	−15.0 (18.4) (n = 54)	−25.1 (21.5) (n = 54)	−34.4 (21.9) (n = 53)	−42.1 (21.5) (n = 47)
ARP2	−20.0 (20.4) (n = 22)	−31.7 (20.9) (n = 22)	−43.4 (21.3) (n = 23)	−52.8 (24.3) (n = 19)
ARP3	−8.2 (14.2) (n = 24)	−14.7 (21.2) (n = 24)	−25.7 (23.8) (n = 23)	−31.6 (26.3) (n = 21)
ARP4	−15.9 (17.0) (n = 254)	−26.5 (21.0) (n = 254)	−34.6 (23.0) (n = 251)	−43.9 (23.5) (n = 223)
ARP5	−14.6 (15.6) (n = 170)	−25.7 (21.0) (n = 170)	−34.9 (23.5) (n = 169)	−43.0 (24.5) (n = 146)

AR, allergic rhinitis; ARP, AR subpopulation; SD, standard deviation; VAS, Visual Analogue Scale.

was prescribed for the first time and if their overall symptoms were rated ≥ 50 mm on a Visual Analogue Scale [VAS]. Symptom severity was evaluated by VAS at baseline and days 1, 3, 7, and ≈ 14 (approximately; last day). Patients were assessed by AR phenotype and comorbidities. The AR subpopulations (ARPs) were comprised of the following:

IgE response restricted to one environmental allergen without family history (ARP1):

Polyclonal IgE response to > 5 environmental allergens with family history (ARP2): Nonallergic polyclonal IgE (patients with IgE test, but no increased total IgE value) without family history (ARP3)

Intermediate phenotypes (ARP4): Comorbidities including asthma, food allergy, eczema, or severe allergic reaction (ARP5)

ARP1, ARP2, ARP3, and ARP4 were derived from the classification of IgE-mediated diseases provided by the MeDALL paper [Bousquet J et al. *Allergy*. 2016;71(11):1513-1525].

Results: Patients (N = 450) had a mean age of 41.7 years and 59.1% were female. Mean baseline VAS for overall AR symptoms ranged from 70.9–77.6 mm for all ARPs. MP-AzeFlu was associated with a VAS score reduction from baseline to days 1, 3, 7, and the last day for all ARPs (Table). VAS score reductions from baseline to last day ranged from 31.6–52.8 mm for all ARPs (Table).

Conclusion: MP-AzeFlu provided effective and rapid symptom control in patients with AR, irrespective of AR phenotype or comorbidity, supporting MP-AzeFlu as an effective treatment for patients with moderate-to-severe AR.

TP1546 | Functional activity of blood phagocytes in response to methicillin-resistant strains of staphylococcus aureus

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Background: Here we compared phagocytic activities of blood monocytes upon exposure to strains of methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-susceptible *S. aureus* (MSSA).

Method: Blood monocytes were collected from 25 healthy adults (age: 25–45 years). Live suspensions of MRSA/MSSA strains were used at a concentration of 10^6 colony-forming units (CFU)/mL. Phagocytic activities of blood monocytes of varied phenotypes exposed to live suspensions of MRSA/MSSA strains were estimated using flow cytometry based on direct immunofluorescence and lucigenin- and luminol-dependent spontaneous and induced chemiluminescence.

Results: We observed that the *respiratory burst* of monocytes upon MRSA exposure was characterised byan increased production of secondary radicals, causing expression of reactive oxygen species and reduction of primary radicals in the form of the superoxide anion. Further, regarding oxygen-dependent phagocytosis, monocytes with the $CD14^+CD16^-$ phenotype mostly exhibited a higher phagocytic index, and the number of this phagocytic subset was more frequently higher in comparison with that of monocytes with $CD14^+CD16^+$ and $CD14^{low}$ $CD16^+$phenotypes.

Conclusion: Thus, we observed changes in the phenotypic composition and *respiratory burst* intensity of peripheral blood monocytes and an increase in the activity of the whole fraction of monocytes upon MRSA exposure.

TP1547 | Comparative analysis of sequenced mycobacterium tuberculosis DNA genomes with different drug resistance spectra

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Background: The purpose of this study is to determine the genetic variants of Mycobacterium Tuberculosis (MBT) obtained from patients with pulmonary tuberculosis with different spectra of drug sensitivity.

Method: MBT samples were collected from 266 patients with pulmonary and extrapulmonary tuberculosis with different spectra of drug resistance (39 patients with sensitive, 5 patients with Monoresistant (MonoDR), 3 patients with Polyresistant (PolyDR), 161 patients with MultiDrug Sensitivity (MDR), 58 patients with XDrug Sensitivity (XDR)TB). Different types of pathological material were used for the study: sputum, bronchoalveolar lavage, ascitic and pleural fluid, biopsy materials, etc. Genotyping of selected MBT samples was carried out by phenotypic (BactecMGIT - seeding on liquid media; seeding on Levenshtein-Jensen solid media) and molecular genetic (GenoType MTBDRpl and GenoType MTBDRsl) methods. To study the genomic chain, DNA sequencing was performed.

Results: As a result of the studies, the types of sequenced mycobacterial strains and the frequency of their isolation were identified, both in the general group of patients and among patients with various types of drug sensitivity. 15 species of sequenced strains were identified. The most common: Beijing-187 (70%); T1-31 (12%); H3-14 (5%); LAM9 - 10 (4%). The remaining 11 types of sequenced strains - LAM5; LAM9, T1; T1-RUS1; T5-RUS2; T2; T2, H3, T3; T4; MANU2; MANU2, H3; CAS; UNKNWN - were isolated from 24 patients, which accounted for only 9% of the total number of the patients examined (266). The distribution of the Beijing strain was analyzed among patients with different spectra of drug sensitivity. The results are as follows: MDR-114 (70%), XDR-46 (79%), MonoDR-3 (60%), PolyDR-3 (100%), Sensitive-21 (54%). The obtained results imply that the Strain Beijing prevails for all tuberculosis patients, independently of the spectrum of drug resistance.

Conclusion: The results of a molecular genetic study of 266 DNA samples isolated from Mycobacterium Tuberculosis, obtained from

patients with tuberculosis with various types of drug sensitivity, showed that the Beijing strain is identified in the vast majority of cases (70%).

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TP1548 | Parasitic hyperinfection

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Case report: A 62-year-old patient derived for eosinophilia.

Pathological history: chronic rhinosinusitis with nasal polyps. Bronchial asthma diagnosed more than 10 years ago. Diagnosis of hypereosinophilic syndrome with expression Chronic eosinophilic pneumonia clinic since 1996 (2-3 episodes that go requiring hospital admission and good evolution with long-term corticosteroids). Apparently stable to date. Natural of Spain, no trips abroad. Reason for consultation: Last 2 hospitalization in January and March 2015 for severe persistent asthma eosinophilic fever of 39° C, chills, asthenia, dyspnoea of progressive effort and cough with greenish expectoration. Refractory to ambulatory treatment with amoxicillin/clavulanic and quinolones, enter for acute respiratory insufficiency. Concomitantly It refers to diarrheal depositions without pathological products that have been self-limiting, nausea with vomiting of food content. It has no history of colonization bacterial or fungal. Complementary Explorations: The chest tomography exhibits consolidation opacities bilateral pulmonary and a pattern of organized pneumonia. During post-entry control, Eosinophilic blood has been observed since 2009, which is oscillating between levels within the limit of the normality up to maximum levels of 1200 eos/mm^3, associated to total IgE 7500 UI/mL.

It is derived from allergology, where an allergic study is conducted with an allergic prick test inhalants and foods with a negative result, normal immunoallergic analytical, study of parasites, including positive serology to Strongyloides estercoralis, and parasitic culture in feces that confirm the presence of this microorganism.

Diagnostic guidance, treatment and evolution: It is oriented as a Löffler Syndrome (pulmonary infiltrates of eosinophilic origin) secondary to parasitic hyperinfection per Strongyloides stercoralis. It is treated with ivermectin, negativizing the serology and the coproductions After the treatment has finished, the patient has not returned to present Peripheral eosinophilicity in blood or new events of eosinophilic pneumonia.

TP1549 | Eczematous reaction in scabies-when to treat?

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Case report

Background: Eczema can be as a pre-existing skin disease, that mostly affects children; it can be induced by local treatment or, it can develop as a result of the patient being infested with scabies mites. Scabies is a skin condition caused by the mite Sarcoptes scabiei. Clinically described as intense itching, scabies is very contagious and spreads quickly through close physical contact in the community. Scabies can cause widespread eczema, manifested as an important cutaneous reaction caused by an imbalance between the patient's immune reaction and mites. This type of eczema can become secondarily infected and thus aggravating the prior eczematous reaction [1]. Topical treatments are available and effective measures in treating scabies. However, they can induce irritant skin reactions, especially in small children or in immunocompromised patients. According to recent guidelines, scabies can be treated with topical permethrin, benzyl benzoate, malathion, lindane or crotamiton for killing scabies mites as the first stage; emollients and topical steroids with or without antibiotics should be recommended for eczematous reactions afterwards [2].

Method/Results: We present a series of cases that exemplify severe eczematous reactions in patients diagnosed and treated for scabies. This indicates that the first line of treatment should be steroids followed up by scabies therapy.

Conclusion: We propose that in the case of eczematous scabies, the first line treatment should be topical and/or systemic steroids, followed by the therapy for scabies.

References: 1. McCarthy JS, Kemp DJ, Walton SF, Currie BJ. Scabies: more than just an irritation. Postgrad Med J 2004;80: 382-7.

2. Johnston G, Sladden M. Scabies: diagnosis and treatment. BMJ. 2005;331(7517):619-22.

TP1552 | A case of resolution of Melkersson-Rosenthal following a dental treatment

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Case report

Rationale: Melkersson-Rosenthal Syndrome (MRS) is a rare neurological disorder. Cheilitis, facial paralysis and a fissured tongue are pathognomonic of MRS. Depending on the individual, episodes vary in degree and length. However, for all individuals the severity of the symptoms increases with each progressive episode and can

eventually become permanent. Symptoms associated with MRS impair senses causing visual disturbances and diminishment of taste in the mouth.

Methods: Surgical pathology of a specimen from the right upper lip.

Results: A 77-year-old woman presented with daily swelling in the upper lip, gums and tongue. Onset of symptoms occurred approximately 4-5 years ago. Biopsy showed presence of nonnecrotizing granulomatous inflammation in the upper lip, prognostic of MRS. However, it is noted that there is an absence of facial paralysis, producing an incomplete expression of MRS. She was prescribed prednisone 5 mg in hopes of suppressing the swelling. However, this was discontinued as it has proven ineffective in cases of MRS.

As a result of chain smoking for many years, she had developed periodontitis, otherwise known as inflammation of the gums. Consequently, to allow the gums to heal before implants were put into place, she underwent a dental procedure to remove her four frontal teeth. Subsequently, the swelling subsided significantly and no episodes have presented since. She has experienced full resolution of MRS symptoms following the dental procedure. The etiology of MRS is still unknown, but in this case, it is hypothesized to be a low-grade infection in the mouth.

Conclusions: While antibiotics, steroids and surgical resection have been used, we suggest that in cases of MRS associated with periodontitis, treatment of the focal dental infection should be explored.

TP1553 | Evaluation of the sensitization profile in patients with chronic allergic persistent rhinitis complicated by relapsing herpes simplex virus type 1

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Background: To determine the profile of sensitization in patients with chronic persistent allergic rhinitis (CPAR) complicated by relapsing Herpes simplex virus type 1 (HSV-1) in the level of sIgE.

Method: Determination of sIgE was performed by ImmunoCAP Phadia (Thermo Fisher). The study involved 162 patients who applied for a consultation to the Clinic of Immunology and Allergology "Forpost" in Kyiv. Among them, 122 patients suffered from frequent relapsing HSV-1 (exacerbations were more than 5 times a year) and 40 patients from moderately.

Results: Analyzing the spectrum of sensitization in groups of patients with CPAR from frequent relapsing HSV-1 showed that sensitization to mold allergens was most commonly found and it was found in 106 patients (86.88%). Among them, 56 patients (45.9%) had sensitization to HDM and fungal allergens at the same time. Sensitization to HDM occurred in 99 patients (81.14%). In 32 patients (26.23%) poly-sensitization was determined. In 47 patients (38.5%) sensitization to epidermal allergens was detected, but only 2 patients (1.6%) had mono-sensitization. Among fungal allergens in a majority sensitization to Alternaria alternata was detected in 102 patients (96.2%), as mono-sensitization in 92 patients (86.8%). Sensitization to other mold fungi was occurred with Alternaria alternata to Penicillium notatum - in 4 patients (3.8%), to Cladosporium herbarum – in 9 patients (8.5%), to Aspergilius fumigatus – in 6 patients (5.7%), to the opportunistic yeast fungus Candida albicans - in 10 patients (9.4%). In the analysis in the group of patients with CPAR from moderately relapsing HSV-1, were revealed: sensitization to mold was found in 7 patients (17.5%), to HDM in 12 (30%), to epidermal allergens in 6 (15%) and to pollen in 15 patients (37.5%).

Conducting the determination of the level of sIgE revealed that in the group of patients with the CPAR from frequent relapsing HSV-1 the most important allergens were fungal and HDM allergens, the incidence rate was 86.88% and 81.14% respectively. Whereas in the group of patients with CPAR from moderately relapsing HSV-1 the most significant allergens were HDM and pollen (30% and 37.5%) respectively.

Conclusion: Thus, it was found that in the group of patients with CPAR from frequent relapsing HSV-1, the characteristic causative allergens were fungal allergens, HDM and, to a lesser extent, epidermal and pollen allergens. The most common relapses of HSV-1 type were in patients with co-sensitization to mold and HDM at the same time.

TP1554 | The effect of mycoplasma pneumoniae on the clinical course of bronchiolitis in children

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Background: To assess the effect of Mycoplasma Pneumoniae on the clinical and immunological parameters in children with bronchiolitis

Method: Surveyed 136 children with bronchiolitis at the age from 1 to 15 years. In 39 patients, the results of the study of mycoplasmal infection were positive. The concentration of specific IgG and IgM for mycoplasma pneumoniae was determined using enzyme immunoassay. The phenotypic composition of peripheral blood lymphocytes (CD3, CD4, CD8) is evaluated by the method of indirect immunofluorescence for the presence of membrane antigens.

Results: In patients with mycoplasmal infection, the exacerbation of the pathological process was characterized by the brightness of the manifestations. Indicators such as the frequency of exacerbations, the duration of BOS, the degree of hyperthermia, the duration of cough were evaluated. Symptoms of intoxication were expressed. Broncho-obstructive syndrome, shortness of breath, spastic paroxysmal cough, the participation of auxiliary muscles in the act of breathing on the background of hypothermia severity. Auscultation:

diffuse dry whistling and buzzing and moist small-caliber rales. A chest radiograph showed an increase and deformation of the bronchopulmonary pattern, expansion of the roots, and the phenomenon of peribronchitis. However, the duration of these symptoms was short. The study of cellular immunity showed a decrease in helper activity of T cells in the acute phase. The suppressor activity was also characterized by a pronounced decrease: CD3 (54.5 ± 0.3 $P > 0.05$), CD4 (34.6 ± 0.2 $P < 0.05$), CD8 (22.6 ± 0.4 $P > 0.5$), CD4 / CD8 (1.62 ± 0.03 $P < 0.01$).

IgG concentration at mycoplasma infection in the acute stage -0.59 ± 0.03, IgM level: 0.67 ± 0.04

Conclusion: The presence of mycoplasma infection in the genesis of the disease contributes to the long course of bronchial obstruction syndrome with frequent relapses. A moderately pronounced immunosuppression of the cell type in the acute stage was noted.

TP1556 | Bacterial agonists of innate immunity LPS regulates spontaneous and induced production of alfa defensins of human neutrophils in vitro

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Background: Neutrophils recruitment is an important factor for the development of allergic inflammation. Allergens recruit neutrophils in a TLR4, MD2 and CXCR2-dependent manner. Neutrophils are the major effectors of acute inflammation responding to tissue injury or infection, releasing a large number of antimicrobial peptides alpha-defensins. The most common of these peptides is HNP1 (human neutrophil peptide 1). Alpha defensins reduced during using norepinephrine that often used during allergic diseases reduce antimicrobial functions and facilitate the spread of infection. The purpose of this study was to investigate the effect of noradrenaline on spontaneous and lipopolysaccharide-induced alpha defensins production by human neutrophils in vitro.

Method: Neutrophils were collected from 43 healthy donors and were isolated by two methods, as follows: by density gradient centrifugation of whole blood, dextran sedimentation and red cells osmotic lysis (Neu1); similarly to Neu1, but with an additional immunomagnetic negative selection step, using the EasySep Human Neutrophil Enrichment Kit (Neu2). According to morphological analysis and flow cytometry 92-98% pure neutrophils were in Neu1 and > 99% was in Neu2. Neutrophils (1×10^6 cells/mL) were incubated in medium RPMI 1640 (37°C, 5% CO2, 20 h) with DPBS or 10 ng/mL lipopolysaccharide (LPS), noradrenaline (0.1 μM). Total RNA was extracted and then analyzed by RT PCR for alfa-defensin - Human Neutrophil Peptide 1 (HNP1).

Results: Noradrenaline decreased production only of alfa-defensin - Human Neutrophil Peptide 1 (HNP1) by non-stimulated neutrophils in Neu1 ($P < 0.05$) Adrenaline did not effect on spontaneous and LPS-induced secretion of alfa-defensin - Human Neutrophil Peptide 1 (HNP1) by neutrophils in Neu1 and Neu2.

Conclusion: Catecholamine noradrenaline decreases spontaneous production of proinflammatory of alfa defensins by human neutrophils in vitro. 2. LPS upregulates decreased level of alfa defensins. 3. Experimental data support the evidence that alfa-defensin - Human Neutrophil Peptide 1 (HNP1) expression is regulated by TLR signaling in human neutrophils.*The publication has been prepared with the support of the "RUDN University Program 5–100"

TP1557 | Broad spectrum of autoantibodies in a malaria infected patient: Are they harmful or protective for an infected host?

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Case report

Introduction: It is well known that parasitic infection, such as malaria, may trigger autoantibodies (AAb) production. We report a case of a 35-years old, male patient with malaria, who developed a broad spectrum of AAb.

Results: The patient was complaining of intermittent fever (up to 40C), malaise, loss of appetite and weight loss, dark urine and yellowish sclera discoloration that lasted for several weeks. Laboratory analysis showed elevated ESR (74 mm/h), CRP (168 mg/L), fibrinogen (4.8 g/L), procalcitonin (5.75 ng/mL), anemia (hemoglobin 80 g/L), high serum concentration of LDH and bilirubin, and positive direct and indirect Coombs test. Abdominal ultrasound revealed enlarged spleen and liver. After initial evaluation in a local hospital, infective and hematological etiology was excluded and he was referred to our clinic for further evaluation in August 2017. Multiple AAb positivity was found: ANA of homogeneous pattern (1:80), anti-histone antibodies (Abs) (20.3Ru/mL), extremely high concentration of anticardiolipin (193.6U/mL) and anti-beta 2 glycoprotein Abs (308.7U/L), both of IgM isotype. In addition, positive anti-smooth muscle Abs (1:80) and ANCA directed to Elastase (59.5U/mL) and Lysozyme (29.7U/mL) were found. Myositis profile showed positivity to PmScl 75 (+++), PL-7 (+), PL-12 (+++), Mi-2 (+), Ku (+), SRP (+), EJ (+). An elevated gamma globulin fraction (27.3% of total protein) in serum protein electrophoresis and high concentration of total IgE (1600 IU/mL), IgG (18.8 g/L), IgM (13.26 g/L), IgA (4.96 g/L) and low C4 (0.087 g/L) were found.

Repeated peripheral smear examination, done by our hematologist in Clinical Center of Serbia, revealed ring forms of *Plasmodium vivax*. The patient was found to have malaria and sent to Clinic for Infective Disease, where he was treated with antimalarians and steroids. The

therapy led to a complete recovery of the patient. A year later, the patient was well and his complete immunological serologic tests were within normal range.

Conclusion: Malaria may trigger the production of many different AAb. There are still many questions regarding their development and potential harmful or protective effect for an infected host.

TP1558 | Dietary intervention with a BbC50 fermentation product promotes the adaptive immune response in a murine influenza vaccination model

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Background: Specific fermentation products were shown to have immunomodulatory effects in clinical and preclinical trials (Granier A. et al., 2013). The aim of this study was to determine the effect of a dietary intervention with BbC50 fermentation product on the vaccine responsiveness in a murine influenza vaccination model.

Method: C57BL/6JOlaHsd female mice (6 week-old) received a primary and booster influvac vaccination on day 0 and day 21, after which vaccine-specific delayed-typed hypersensitivity (DTH) was measured. Two weeks prior to start, mice were fed a diet supplemented with 0.5% or 2.5% (w/v%) BbC50 fermentation product until the end of the experiment. In addition, lactose control groups were included (0.25 and 1.25% w/v%). Immune cell populations of the spleen were analyzed using flow cytometry and co-cultured with influenza loaded bone marrow-derived dendritic cells (BMDC).

Results: The vaccinated mice showed an influvac specific DTH response as compared to the non-vaccinated sham mice. Dietary supplementation with BbC50 fermentation product, showed enhancement of the DTH response, reaching significance at 2.5% as compared to mice fed lactose as a control ($P < 0.05$).The ferments did not further enhance influenza specific IgG1 and IgG2 in serum, nor IFN-g and IL-13 levels in the co-culture supernatant. The 1.25% lactose control diet was found to enhance the frequency of activated cytotoxic T-cells as well as B-cells in the spleen, and tended to lower the regulatory T-cell frequency. By contrast, the 2.5% BbC50 fermentation product tended to restore the percentage of activated Th1 ($P = 0.0546$) as compared to the levels of sham control mice.

Conclusion: Dietary intervention with BbC50 fermentation product was able to boost the adaptive immune response in an influenza vaccination mouse model as measured by DTH. Future studies should provide further insights regarding the mechanism by which the fermentation products are able to modulate immune responses.

TP1559 | Peripheral blood neutrophil and monocyte activation test for the differential diagnosis of bacterial versus viral etiology of acute intestinal infections

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Background: The differentiation between viral and bacterial etiology of acute intestinal infections (AII) is difficult, various protocols using C-reactive protein, MMP-9, sICAM-1, procalcitonin, band count and others as biomarkers of bacterial infection. This study assesses a new method to determine the etiology of acute intestinal infections.

Method: Approval of Bioethical Committee was obtained and the study was registered on ClinicalTrials.gov (NCT03161951). Venous blood (3 ml) was taken from patients with acute intestinal infections (n = 116, viral origin – 48, bacterial – 68) and healthy controls (n = 18) from a cubital vein into a vacutainer containing EDTA. The expression of Fc-receptors (CD64, CD16) and L-selectin (CD62L) on the surface of neutrophils and monocytes was assayed by flow cytometry. The percent of expression CD16 on the surface of blood monocytes, relative fluorescence intensity (RFI) of CD62L on the surface of neutrophils and monocytes and both for CD64 on neutrophils were analyzed.

Results: Expression of all studied molecules on the surfaces of neutrophils and monocytes in the blood of the patients with acute intestinal infections and healthy donors were performed. ROC analysis was conducted to establish the sensitivity, specificity and threshold value of each parameter in the detection of bacterial infections among all acute intestinal infections. Among all parameters those with best ratio of sensitivity and specificity were selected for detecting bacterial etiology: CD62L (RFI, neutrophils and monocytes.), CD64 (RFI and %, neutrophils), CD16 (%, monocytes). The diagnostic criteria for bacterial etiology are the following values of parameters: CD62L (RIF, neutrophils) - above 145.4; CD62L (RIF, monocytes) - above 159.1; CD64 (RIF, neutrophils) - above 19; CD64 (%, neutrophils) - above 44.0%; CD16 (%, monocytes) - above 59.0%. If a patient has values of at least 3 out of 5 analyzed parameters which correspond to the above diagnostic criteria, treatment is prescribed for acute intestinal infections of bacterial etiology. If a patient has values of 2 or less parameters that meet the above diagnostic criteria, treatment is prescribed for acute intestinal infections of viral etiology.

Conclusion: Expression of CD62L, CD64 and CD16 on the surface of neutrophils and monocytes in the blood can be used as markers for the differential diagnosis of bacterial and viral etiology of intestinal infections.

TP1560 | Expression of immune system genes in patients with meningococcemia

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Background: One of the most serious and life-threatening infectious diseases is bacteremia and septic shock. Neisseria meningitidis (Meningococcus) is an important bacterial infection manifesting as meningitis often with septicemia.

Method: Peripheral blood mononuclear cells from 18 patients age 19 and 54 years with meningococcemia and from a control group of 32 healthy persons were obtained. Total RNA was isolated from the mononuclear cells using Tri-Reagent (Sigma, USA). cDNA was synthesized using the Superscript cDNA Synthesis Kit (Invitrogen, CA). Subsequent quantitative real-time polymerase chain reaction (qPCR) was performed using the GoTaq®qPCR Master Mix with BRYT Green (PROMEGA, USA). The efficiency of amplification for each primer (*ACTB*,*GAPDH*,*CD86*,*MD2*,*CD14*,*CD6*,*CD8*,*TLR2*,*TLR4*,*TNF*,*IFNG*) was determined. Hybridization of labeled cDNA was carried out on a biochip (96 genes) Arrayit Dendritic & Antigen Presenting Cell Pathways Microarrays (n = 26) with scan to Innoscan 700 (Carbon, France).

Results: Combined expression of genes is slightly greater in the control group of patients. Genes were identified with significant differences ($P < 0.05$) in the expression level between the meningococcemia patients and controls: MD2,CD14,CD6,CD8,TLR2,TLR4,TNF,IFNG. In meningococcemia patients highly expressed genes included MD2 ($P = 0.0383$), CD14 ($P = 0.019$), CD6 ($P = 0.0232$), CD8 ($P = 0.041$), TLR2 ($P = 0.0434$), TLR4, ($P = 0.0021$), IFNG ($P = 0.0031$). Lower expressed genes are CD1A ($P = 0.0398$), IL2 ($P = 0.04$), CD1D ($P = 0.021$). Genes up regulated include: TLR2; while down regulated are: CD14,CD6,CD8.

Conclusion: This study analyzed the expression of 96 of the most significant genes of the immune system. In patients with meningococcemia high and low expressed genes were identified, as were genes whose expression is significantly different in meningococcemia patients versus healthy individuals. Meningococcus induces significant activation of the immune responses.

TUESDAY, 4 JUNE 2019
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TREATMENT OF FOOD ALLERGY

TP1561 | Does oit protocol for milk allergy really change dietetic patterns?

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Background: The elimination diet for milk allergy leads patients to potential nutritional and growth deficiency and limitations in social life. Oral immunotherapy(OIT) for milk allergy seems to be a valid alternative in protecting patients from accidental exposure, in improving nutritional status and quality of life. In our study we analysed how the milk allergic patients diet changes after an OIT protocol.

Method: 16 patients (7 -22 years old) affected by cow's milk allergy and no other food allergy were included. All patients were evaluated using two 7 days food diary records: One during exclusion diet, when they were supported by a dietitian, and the second three months after the OIT completed (free diet diary) without any nutritional support. All data collected were analysed using a nutritional software (Gedip Solution) and compared with the LARN Italian Guidelines 2014.

Results: In both evaluations each patient did not cover nutritional requirements according to RDA and there were not statistical differences between two evaluations. We noticed a greater gap in the second evaluation, probably linked to the absence of a nutritional support. Assessing the impact of milk and derivatives after OIT in nutritional intake this were the results: 19% of proteins, 19% of lipid and 65% of calcium amounts were provided by milk. Analysing in detail milk products assumption after OIT, we found that patients preferred hard cheese (94%), soft cheese (75%), pizza (62%), yogurt (56%) and they consumed less sweet food like chocolate (12%), ice-cream (12%), pudding (6%). Despite all patient were prescribed to drink fresh milk daily to maintain tolerance, 25% of them did not take it at all.

Conclusion: Our preliminary data suggest that, also after OIT protocol for milk allergy, some nutritional deficiencies may exist. A dietetic support could be useful in order to improve the nutritional profile and to successfully introduce all milk products in daily meals. More studies with a large sample and a control group are needed also to evaluate the effects in the short and long term.

TP1562 | Oral immunotherapy (OIT): Efficacy and safety in a group of children with cow's milk allergy

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Background: Oral Immunotherapy (OIT) provides a treatment option for children with severe food allergy. The aim of this study is to assess the safety and efficacy of an OIT protocol conducted in hospital on a group of children with severe allergy to CM.

Method: In this retrospective study children aged 2-11 years with severe/persistent CM allergy were included. They underwent a personalized OIT protocol with monthly incremental steps over 3 consecutive days. According to the amount of CM consumed, they were classified as: Tolerant (>120 ml CM), Partially Tolerant (<120 ml CM), Failure and Drop-out. Total(t)/Specific(s) IgEs and Skin Prick Tests (SPTs) were analyzed along with any adverse reactions during OIT procedure.

Results: Twenty children were included in the study, mean aged 6.9 ± 2.5 years (75.0% male) [tIgE: 1034.1 ± 1096.6KUA/L; F2: 85.7 ± 71.5KUA/L; F76: 28.3 ± 40.2KUA/L; F77: 24.2 ± 34.2KUA/L; F78: 79.7 ± 66.4KUA/L, SPT.CM: 10.7 ± 3.4 mm]. A history of anaphylaxis to CM was reported in 16 children (80.0%).

Thirteen children (65.0%) achieved tolerance and 2 (10.0%) partial tolerance (Mean daily CM consumption of 153 ml and 26 ml respectively). One child (5.0%) failed to complete the protocol due to recurrent anaphylactic episodes and 2 (10.0%) due to doctor diagnosed eosinophilic esophagitis. One dropped out and 1 is ongoing with the treatment.

Eight children (40.0%) had not presented any side effects during OIT [tIgE: 476.8 ± 434.2KUA/L; F2: 42.8 ± 48.7KUA/L; F76: 15.5 ± 42.6KUA/L; F77: 7.6 ± 13.6KUA/L; F78: 42.6 ± 44.6KUA/L; SPT.CM: 11.0 ± 4.9 mm], while 7 (35.0%) had manageable anaphylactic reactions [tIgE: 1858.1 ± 1372.1KUA/L, F2: 101.1 ± 59.2KUA/L, F76: 33.3 ± 37.8KUA/L, F77: 27.0 ± 33.1KUA/L, F78: 120.5 ± 86.6KUA/L, SPT.CM: 10.0 ± 1.3 mm]. Five children (25.0%) had mild allergic reactions: Urticaria (3; 60.0%) and OAS (2; 40.0%) [tIgE: 772.2 ± 814.0KUA/L; F2: 132.6 ± 96.4KUA/L; F76: 42.1 ± 41.7KUA/L; F77: 46.7 ± 48.8KUA/L; F78: 82.0 ± 24.0KUA/L; SPT.CM: 11.0 ± 3.2 mm].

High levels of tIgE were linked with increased probability of reactions ($P = 0.032$). Borderline correlation was recorded for F2 ($P = 0.07$) and F78 ($P = 0.07$), probably due to small sample size.

Conclusion: OIT is an effective treatment in the majority of children with severe CM allergy, inducing tolerance and improving quality of life though it should be conducted in specialized centers by accordingly trained personnel since severe anaphylactic reactions or eosinophilic diseases might occur.

TP1563 | Single-centre investigation of appropriate maintenance dose in rush oral immunotherapy for severe milk allergy

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Background: Risks of symptoms have been noted during oral immunotherapy. We aimed to determine safe and effective maintenance doses of rush oral immunotherapy (ROIT) in patients with severe milk allergy.

Method: Patients with positive oral food challenge test (OFC) results with milk were included in this study. The median age of the patients was 6 (5-15) years, and the median final OFC dose of milk was 2 (0.01-10) ml. Thirty-three patients were randomly assigned to one of two groups according to the maintenance target dose: 20-ml group (n = 17) or 100-ml group (n = 13). The milk doses were administered to subjects in the hospital and were gradually increased to the target dose. Then, subjects were exposed to maintenance doses daily for 6 months at home. At 6 months after discharge, OFCs with milk were performed. The primary endpoint was the OFC final dose at 6 months. Adverse events during ROIT were evaluated.

Results: The median OFC final dose at 6 months was 10 (2-100) ml in the 20-ml group and 15 (2-100) ml in the 100-ml group; there was no significant difference between the two groups ($P = 0.867$). During the rash increasing and maintenance phases, the median times of skin symptoms in the 20-ml group were 3 (0-9) times and 4 (0-31) times, respectively, compared to 6 (1-18) times and 7 (0-17) times in the 100-ml group; the times of skin symptoms were significantly lower in the 20-ml group than in the 100-ml group in both phases ($P = 0.015$ and $P = 0.03$, respectively). During the maintenance phase, 1 patient in the 20-ml group were administered adrenaline 1 time, compared with 5 patients in the 100-ml group administered adrenaline 6 times total. The times of adrenaline use in the maintenance phase was significantly lower in the 20-ml group than in the 100-ml group ($P = 0.006$).

Conclusion: The increase in threshold was nearly equal when using maintenance doses of 20 ml and 100 ml in ROIT for patients with severe milk allergy. The risk of adverse symptoms was considered to be lower in patients who received maintenance doses of 20 ml. Thus, a maintenance dose of 20 ml is considered appropriate for both safety and effectiveness.

TP1564 | A phase 2 randomized controlled study using omalizumab as an adjunct therapy during multi-allergen oral immunotherapy in food allergic individuals to test long-term outcomes

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Background: Currently, there is limited data on the sustainability of desensitization of multi-food oral immunotherapy (OIT). We conducted a multi-food OIT study at multiple sites to compare the persistence of tolerance with variable OIT dosing after reaching maintenance in multi-food OIT.

Method: We enrolled 70 participants, aged 5-22 years with multiple food allergies confirmed by double-blind placebo-controlled food challenges (DBPCFCs). In the open-label phase of the study, all participants received omalizumab (weeks 1-16) and multi-OIT (2-5 allergens; weeks 8-30). All participants on a maintenance dose of each allergen by week 28-29 were randomized 1:1:1 to receive 1 g, 300 mg, or 0 mg protein of each allergen in a blinded fashion (weeks 30-36) and then tested by DBPCFC at week 36. Success was defined as passing 2 g food challenge to at least 2 foods at the week 36 challenges.

Results: Most participants were able to reach a dose of 2 g or higher of each of 2, 3, 4, and 5 food allergens (as applicable to the participant's food allergens in OIT) during week 36 food challenges. Using an intent-to-treat analysis, we did not find evidence that a 300 mg dose was effectively different than a 1 g dose in maintaining desensitization, and both were more effective than OIT discontinuation (0 mg dose) (85% *vs* 55%, $P = 0.03$). Fifty-five percent of the intent-to-treat participants and 69% of per protocol participants randomized to the 0 mg arm showed no objective reactivity after 6 weeks of discontinuation. Cross-desensitization was found between cashew/pistachio and walnut/pecan when only one of the

foods was part of OIT. No statistically significant safety differences were found between the three arms.

Conclusion: These results suggest that sustainability of desensitization is best achieved after multi-OIT with adjunct omalizumab therapy through continued maintenance OIT dosing of either 300 mg or 1 g of each food allergen, as opposed to discontinuation of multi-OIT.

TP1565 | Real-life efficacy of omalizumab in children with severe allergy to multiple foods

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Background: The impact of omalizumab on food allergy are poorly studied out of the context of oral immunotherapy. This real life study aims to assess the effect of omalizumab on food tolerance in pediatric patients treated for severe asthma.

Method: We review the food thresholds of patients with severe asthma and anaphylactic reactions to at least 2 different foods before and after a 4-month-long Omalizumab treatment. We also report their asthma control and quality of life, measured by PedSQL.

Results: Fifteen children -allergic to 37 foods- got a threshold increase for milk, egg, wheat and hazelnut from 1221.1 ± 1736.7 mg (mean ± standard deviation) to 8553.7 ± 8063.6 mg eliciting dose ($P < 0.001$) [Table 1]. Patients reached full tolerance for 70.4% of the tested foods, which were re-introduced in the patients' diet without necessity of oral immunotherapy procedures. The remaining foods were partially tolerated. The number of reactions to unintended ingestion of allergenic foods over 4 months dropped from 47 to two. The PedSQL increased from 60.47 ± 5.32 to 87.25 ± 7.33 (parental judgement; $P < 0.001$) and from 62.99 ± 7.39 to 89.71 ± 4.54 (patients' judgement; $P < 0.001$). Omalizumab costed a mean of € 1311.63 per month.

Conclusion: Thresholds of foods reactivity increased by 7 times during Omalizumab treatment for severe uncontrolled asthma. The patients' quality of life increased, due to better asthma control and reduction of dietary restrictions. The cost/benefit ratio of such treatment for selected cases of severe food allergy remains to be evaluated.

TP1566 | Oral immunotherapy for 7 patients with sesame allergy

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Background: Sesame is an important allergen that affects less than 1% of individuals and which has been increasingly reported worldwide. Sesame allergy (SA) begins early in life and persists in 80% of the patients. Allergen-specific immunotherapy has been expected as a possible disease modifying treatment for SA. However, there are few reports about oral immunotherapy for sesame allergy.

Method: In 2016 to 2018, we conducted rush oral immunotherapy (ROIT) for seven children (median age: 10 years) suffering from SA. Before ROIT, 6 patients had suffered anaphylaxis with less than 0.2 g of sesame protein in a cumulative oral food challenge. In the 2 weeks of the rush phase, the patients took increasing doses of sesame paste 2 to 4 times per day. The target dose was 0.6 g of sesame protein. In the maintenance phase, patients consumed the target dose once a day. After at least six months of the maintenance phase without allergic symptoms, we conducted an exercise provocation test (EPT) after consuming the target dose. Afterward, the patients slowly reduced their frequency of intake.

Results: In the rush phase, all patients achieved the target dose, which corresponded to a 15-fold increase in the reaction threshold. The frequency of allergic symptoms that required any medicine was 3.3% (for the total intake); no patients required epinephrine injection. During the maintenance phase, only 1 patient reported oral symptoms during the first six months; however, the prevalence gradually decreased. EPTs have been performed in 6 cases thus far, with only 1 case showing partial urticaria, which did not require medication. Six patients who continued the immunotherapy for more than 1.5 years were consuming sesame freely in their regular diet without reaction.

Conclusion: ROIT is an effective and safe method for treating SA.

TABLE 2. Thresholds of food reactivity tested before and after the treatment with omalizumab in study population (n = 15)

Food	Basal positive, n	Final positive, n	Basal threshold (mg, mean ± SD)	Final threshold (mg, mean ± SD)
Baked egg	1	0	3332	9520
Egg	6	1	1970.8 ± 2802.6	13660.7 ± 9135.8
Baked milk	5	1	1576.4 ± 1473.4	6855.6 ± 812.4
Milk	10	6	731.4 ± 1338. 2	3963.7 ± 3191.7
Wheat	3	0	866.7 ± 293.1	10053.3 ± 600.4
Hazelnut	2	0	8.3 ± 7.8	17695.7 ± 24935.8
Total	27	8	1221.1 ± 1736.7	8553.7 ± 8063.6

TP1567 | Safety and efficacy of sesame oral immunotherapy

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Background: Sesame is becoming increasingly popular in the western diet, making its avoidance, for sesame-allergic patients, challenging. Information regarding the efficacy and safety of sesame oral immunotherapy (OIT) is lacking.

Method: Sixty sesame-allergic patients aged ≥ 4 years were consecutively enrolled into OIT between 11/2014-11/2017. Fifteen sesame allergic patients served as observational controls. Sesame allergy diagnosis was based on a positive oral food challenge or a recent immediate reaction and a positive sesame skin prick test (SPT) or sIgE. Immunological parameters were measured in a subgroup (OIT, n = 16; Controls, n = 11) at the start and end of OIT or observation period. Patients fully desensitized (4000 mg sesame protein) were instructed to consume a daily dose of 1200 mg protein and challenged to 4000 mg after > 6 months.

Results: In the OIT-treated group, 53 patients (88.4%) were fully desensitized to sesame compared to 0% in controls ($P < 0.0001$). Reactions occurred in 4.7% of clinic doses and in 1.9% of home doses during OIT. Epinephrine was used in 12/127 (9.4%) and 7/253 (2.8%) of reactions in hospital and home, respectively. A significant increase in sesame and rSes i 1 IgG4 ($P = 0.001$) and decreases in rSes i 1 IgE ($P = 0.007$) and basophil reactivity ($P = 0.001$) were observed in OIT-treated patients but not in controls. Forty-two patients desensitized to 4000 mg were already > 6 months after reaching maintenance. Only mild reactions were reported during maintenance, and all passed the 4000 mg challenge.

Conclusion: Sesame-OIT is effective but should be performed in specialized centers given the risk of adverse events.

TP1568 | Impact of epicutaneous immunotherapy (EPIT) for the treatment of peanut allergy in children and young adults: Follow-up from the consortium for food allergy research (CoFAR) study

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Background: Peanut EPIT induces desensitization in younger children after 52 weeks of treatment; longer-term outcomes are not well-established. The purpose of this study was to evaluate the potential benefit of extended EPIT for peanut allergic study participants.

Method: Peanut-allergic participants (ages 4-25 years) were randomized to placebo (n = 25), Viaskin Peanut 100mcg (VP100, n = 24), or 250mcg (VP250, n = 25) patch for 52 weeks of blinded therapy, then VP250 for a total of 130 weeks, including crossover of VP100 and placebo-treated participants to VP250. Efficacy was assessed via double-blind, placebo-controlled food challenge (DBPCFC; 5044 mg peanut protein); endpoints included passing the week 130 DBPCFC, successful desensitization at week 130 DBPCFC based on change in successfully consumed dose (SCD) compared to DBPCFC at start of active treatment (success predefined as SCD ≥ 444 mg if starting SCD = 0-44 mg, SCD ≥ 10 times the starting SCD if starting SCD > 44 mg to < 444 mg, and SCD = 5044 mg if starting SCD ≥ 444 mg), and SCD changes at week 130 DBPCFC from DBPCFC at start of active treatment. Adherence, safety and mechanistic parameters were assessed.

Results: At week 130, 18/25 (72%) of Placebo/VP250, 18/24 (75%) of VP100/250 and 23/25 (92%) of VP250 completed treatment. Although no participant passed the DBPCFC, predefined desensitization was achieved in 1/20 (5%) of Placebo/VP250, 5/24 (20.8%) of VP100/250, and 9/25 (36%) of VP250 participants with median SCD change from start of active treatment of 11.5 mg (week 52 = 40 mg), 141.5 mg (week 52 = 43 mg) and 400 mg (week 52 = 130 mg) for each group, respectively ($P = 0.003$ comparing all 3 treatment groups). Median age differences at start of active therapy were noted between groups: Placebo/VP250 (9.4 years), VP100/250 (8.4 years), VP250 (7.7 years). Therapy compliance was > 95% overall. Treatment was well-tolerated with no anaphylaxis and predominantly minor patch-site reactions. Peanut-specific IgG4 and Ara h 2-specific IgG4 increases were observed in all groups over time, with the largest difference noted in the VP250 group; no differences were noted in peanut-specific or Ara h 2-specific IgE levels.

Conclusion: Longer treatment with 250mcg peanut protein could lead to improved outcome of peanut EPIT beyond one year. Safety, tolerability, and compliance findings were reassuring, and mechanistic changes suggest improved immunomodulation with 250mcg peanut EPIT.

TP1569 | AppleCare – birch pollen immunotherapy by consumption of apples

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Background: The majority of birch-pollen-allergic patients develop also an allergy to raw apples and other Rosaceae fruits, known as

oral allergy syndrome (OAS). This can be attributed to a strong homology between the Bet v 1 and Mal d 1 allergens. This cross-reactivity provides an opportunity to use apples in a controlled and established dosage to cure birch pollen- and apple allergy.

Method: Based on *Mal d 1* gene expression analyses, patients (n = 48) with birch-pollen related apple allergy were subjected to a Prick to Prick-Test (PPT) with 23 low, middle and high allergenic apple cultivars. Three apple cultivars of each allergenicity class, selected by oral provocations in 24 patients, are being used in subsequent immunotherapy (SIT). Since October 2018, patients are thereby given a daily defined amount of apple with increasing allergen concentration. ImmunoCAP measurements, Nuclear magnetic resonance (NMR) structure analysis of Mal d 1 isoforms, visual analog scores, pollen-diaries, and conjunctival provocation tests are performed before and after the SIT to assess the tolerability of apples and their impact on birch pollen allergy.

Results: PPTs showed significantly lower wheal and flare reactions on red fleshed and old apple varieties. PPTs also predicted the severity of OAS: symptoms on a red-fleshed apple were lower than on white fleshed. The majority of PPT responses for peeled apple cubes was significantly lower than for unpeeled apple cubes. Results with regard to birch pollen symptoms are expected in 2019.

Conclusion: Besides supporting the assumption that old apple cultivars are better tolerated, we were able to prove the low allergenicity of red-fleshed apples. Now we focus on the SIT with specifically selected apple sorts in increasing allergen concentration because eating fresh apples would be a healthy, time-saving and convenient alternative therapeutic approach to drug-based SIT. Initial results are expected in one year. This Pilot-Study was performed as part of the EU-funded Interreg V-A Italy-Austria 2014-2020 AppleCare-Project.

TP1570 | Nutritional evaluation of patients with successful oral immunotherapy: A strongly recommended procedure

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Background: Cow's milk oral immunotherapy (OIT) has been a common practice in food allergy centers, improving quality of life and reducing the risk of death of allergic patients. However, an overall evaluation of these patients should be considered, since changing food habits can lead to nutritional impairment with long-term consequences. The aim of this study is to describe nutritional assessment of patients undergoing OIT immediately before and one year after procedure.

Method: Retrospective study involving pediatric patients with previous diagnosis of cow's milk protein allergy (CMPA) undergoing cow's milk OIT, from 2012 to 2017. Anthropometric data were collected at baseline (T0), 3 months (T3) and 12 months (T12) after procedure, from medical records. Body mass index ([BMI (kg / m^2) = weight / height^2]) for age was converted into z-score and classified according to World Health Organization (WHO). Patients with no register of weight or height during follow-up were excluded. Ultraprocessed and processed food consumption were described.

Results: 18 patients were enrolled (10 F: 8 M), median age of 9.17 y (5.3-15.6) at baseline. Nutritional evaluation at T0 revealed 12 patients with normal BMI, 4 were overweight and 2 obese (33.3% overweight / obesity). During follow-up, there was a statistical significant increase in mean of BMI (T0 = 17.52; T3 = 18.34; T12 = 19.24) and no significant difference in mean of BMI z-score (T0 = 0.36; T3 = 0.54; T12 = 0.61). Changes in nutritional status occurred in 5 patients, 3 of them varied in both intervals T0 - T3 and T3 - T12. At T3, 3 worsened (overweight to obesity or eutrophic to overweight) and 1 patient improved his nutritional status (44% overweight / obesity). In the period T3 - T12, 3 worsened and nutritional status was improved in 1 patient (38.8% overweight / obesity). Total adherence to treatment (200 ml of daily milk) was referred by 17 patients (94%) at T3 and by 14 (77%) at T12. Ultraprocessed food consumption was referred by 9 (T3) and 11 (T12) patients, respectively and processed food by 4 (T3) and 7 (T12), respectively.

Conclusion: After successful OIT, eating habits can change and lead medical team to a new challenge: the control of overweight. A strict observation and nutritional intervention is mandatory during patients follow-up.

TP1571 | Safety outcomes and differences in eliciting dose upon repeat oral food challenges in multi-food allergic individuals

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Background: Food allergies affect 6-11% of the population across the world, with 40% of affected children having clinical reactivity to more than one food.Oral food challenges (OFCs) are considered the gold standard of diagnosing food allergy. Repeat food challenges

are necessary to assess if food allergies are persistent or outgrown; however, data regarding how allergic adverse reactions change across such repeat challenges is limited.

Method: A retrospective chart review was conducted on all clinical protocols initiated at our institution involving standardized screening OFCs to a cumulative protein dose of 500 mg. Analysis was performed among participants who were challenged to the same food twice at variable time points. Repeat challenges were available for 5 food allergens. Allergic reactions were assessed by modified Bock's criteria and ranked in order of severity by trained allergists.

Results: Twenty-one positive challenges corresponding to 18 participants were analyzed. Sixteen repeat challenges were the peanut, two to egg, and one each to almond, milk, and walnut. While there was no difference in eliciting dose (ED) from the first to second challenge ($P = 0.66$), the AE severity rank significantly increased in the second challenge, corresponding to more severe symptoms experienced ($P = 0.02$).Time between challenges ranged from 2 to 982 days (median 735 days); however, changes in either ED or severity rank were not associated with time between repeat challenges ($P = 0.94$ and $P = 0.56$, respectively).

Conclusion: While individuals experienced similar EDs across first and second OFCs, the severity of occurring AEs increased independent of time between challenges. Our findings could provide better insight into what to expect in performing food challenges in the outpatient clinic setting. Larger cohorts are needed to validate these preliminary findings.

TP1572 | Cow's milk desensitization in a 23-year-old man

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Background: Information on oral immunotherapy (OIT) of cow`s milk (CM) allergy on adults is limited nowadays. Even following a strict diet, patients are not free from suffering a severe accidental reaction.

Method: We report the case of a 22 year-old man, diagnosed since childhood with CM allergy; he developed vomiting and worsening of cutaneous lesions of his atopic dermatitis after CM formula. Allergy was confirmed with skin test (ST) and specific IgE to CM proteins. At the age of 3 year-old an OIT was performed, being unsuccessful because of repeated severe symptoms of anaphylaxis. Therefore, the patient continued avoiding milk until 21 years-old. An allergy workout was performed consisting of ST and specific IgE to CM and its fractions.

Results: SPT were positive with CM and its proteins. Total IgE: 2644 kU/L. Specific IgE (kU/L): CM: 6.8; alpha-lactalbumin: 2.18; beta-lactoglobulin: 0.47 and casein: 7.28. It is well known that higher levels of specific IgE against casein are associated with less efficacy and safeness of OIT. Our patient had a moderate casein level, alpha-lactalbumin and beta-lactoglobulin low levels.

A simple blind oral challenge test (SBOCT) was performed with CM in order to determinate threshold of tolerance. Doses no higher than 45 mg of milk protein (1.5 ml), are a clinical indicator of non-tolerance during OIT. Nevertheless, our patient developed symptoms after a cumulative dose of 4.3 gr (145 mL), being diagnosed of anaphylaxis and needing to be treated with intravenously dexchlorpheniramine, hydrocortisone and 0.5 mg intramuscular adrenaline, recovering after 60 minutes. We began OIT with 70 mL of CM/ diary, with good tolerance during a week, and continued increasing doses to 100, 125, 150 and 200 ml every week, successfully. Seven months later, he is up to now tolerating 200 ml/ diary.

Conclusion: Allergy to ubiquitous food such as CM could be treated in adults.

Patients with severe symptoms and mild to moderate specific IgE levels of casein might achieve tolerance improving their quality of life.

Adults' patients are more likely to be sensitized both to casein and whey proteins than children; therefore, presenting with severe and persistent allergy.

TP1573 | The effect of probiotic supplementation on the acquisition of tolerance to cows' milk protein allergy

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Background: Cows' milk protein allergy (CMPA) is a common childhood food allergy (1)affecting up to 2.4% of children, with the highest prevalence in the first year of life (2)(3). Complications of CMPA have implications for quality of life and health-care costs (1).

Gut microbiota disruption has been associated with the development of allergies(4). Recently there have been efforts to investigate whether probiotics may have a role in the prevention and treatment of CMPA (5). Neonates in units around the United Kingdom routinely receive probiotics to prevent Necrotising Enterocolitis (NEC).

This retrospective cohort study aims to establish whether this routine supplementation in neonates, had a secondary effect on the rates of CMPA in this cohort, and the rate of acquisition of tolerance.

Method: Case records of Neonates born prematurely (≤34 weeks of gestation) at the Royal Devon and Exeter Hospital, United Kingdom, between 2013-2018 who received probiotic supplementation (preparations of *B. bifidum*, *L. acidophilus*or *L. acidophilus*, *B. bifidum* and *B. infantis*) were analysed. Hospital digital notes and document storage databases were scrutinised in order to extract CMPA symptoms or clinician diagnosis of CMPA, as well the analysing the normal 2-year neonatal follow-up data for the age of acquisition of tolerance if CMPA was diagnosed.

Results: Of the 318 neonates included in the study, 25 (8%) were diagnosed with CMPA. The most common symptoms were reflux (28%), vomiting (28%) or both (32%). Of the 25 affected, 10 (40%) patients acquired tolerance within the two years of follow up, whilst 15 (60%) did not. The average age of acquisition of tolerance was 16.3 months.

Conclusion: Considering the background prevalence nationally of CMPA is 2.4%, it was surprising to discover the high prevalence (4.7%) of CMPA in this cohort. However, the average age of tolerance acquisition in this study is much lower than the reported 57% by 5 years of age from longitudinal studies (6). The limited current evidence on probiotics has produced mixed results in the literature and more reliable and relevant data could be obtained from future prospective research, potentially implicating probiotics in speeding up tolerance in CMPA.

TP1574 | Predicting reactions to cow's milk according to specific IgE values in sensitized patients

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Background: Cow's milk allergy (CMA) is the most common food allergy in young children. In order to diagnose this entity, we base the former in the clinical history, skin prick tests, and the determination of cow's milk-specific IgE and the major milk allergens IgE (casein, beta-lactoglobulin, alpha-lactalbumin). Several cut-off values of cow's milk proteins IgE have been investigated to confirm the diagnosis but still not validated in all the populations. Therefore, the challenge test is still the gold standard for diagnosis. The aim of this study is to find an accurate predictor of reactivity in the challenge test based on the measurement of casein and cow's milk-specific IgE.

Method: This is a retrospective study in which we included 99 patients, from 6 months to 10 years of age, subjected to open oral food challenge with cow milk between the years 2012 and 2018, previously diagnosed with CMA at the Ramon y Cajal University Hospital in Madrid, Spain. Casein-specific IgE determination ranged from 0 to 7.34 kU/L and cow's milk-specific IgE determination ranged from 0.01 to 8.3 kU/L.

Results: In our study, 45% of our patients had a positive oral food challenge and 55% had a negative oral food challenge. The best ROC curves were obtained evaluating cow's milk IgE (area under the curve = 0.65) and casein IgE (area under the curve = 0.62). For cow's milk IgE, the confidence interval crosses 1 (95%CI 0.5-1.5), so it made no difference between positive or negative oral food challenges. On the other hand, for casein IgE the OR was 3.65 (95%CI 1.01-13; $P = 0.047$). Considering a 90% specificity, the cut-off point for casein IgE was: 0.5 kU/L. The diagnostic tests with beta-lactoglobulin and alpha-lactalbumin did not improve the accuracy obtained with whole milk and casein tests.

Conclusion: Even though both casein and whole cow's milk IgE have similar discriminatory power, this study suggests that the cut-off point detected for casein revealed a better capacity to predict a reaction during the oral challenge. This result was statistically significant.

TP1576 | Contribution of molecular diagnosis in the prognosis of egg tolerance acquisition

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Background: Egg allergy is considered the 2nd most frequent food allergy in childhood. Ovalbumin (Gal d 2) is the most abundant allergen in egg white and ovomucoid (Gal d 1) the major allergen with the highest allergenicity. Allergic reactions to egg are predominantly IgE-mediated. Our objective was to evaluate the contribution of molecular components (Gal d 1 and Gal d 2) and egg white as prognostic value of egg tolerance acquisition.

Method: Retrospective study in which were selected sera from patients with positive specific IgE (sIgE) to egg white, performed from January 2011 to March 2018. They were divided in groups: Allergic and Tolerant, according to the clinical history at the time of collection, confirmed by oral provocation or egg introduction at home without reaction. sIgE and specific IgG4 (sIgG4) were performed for

	Egg white			Ovalbumin (Gal d 2)			Ovomucoid (Gal d 1)		
	sIgE	sIgG4	sIgE/sIgG4	sIgE	sIgG4	sIgE/sIgG4	sIgE	sIgG4	sIgE/ sIgG4
AUC (%)	84.7	76.3	91.7	85.5	72.4	87.9	70.4	72.7	84.8
Cut-off value	1.56	0.49	0.38	1.03	0.29	0.75	0.99	0.23	0.87
Sensitiv./ Specif. (%)	88/73	63/91	100/73	73/88	54/91	88/82	82/60	79/81	96/82
PPV/NPV (%)	37/97	56/93	40/100	52/95	52/91	46/97	27/95	44/96	48/99

AUC: Area Under the curve; PPV: Positive Predictive Value; NPV: Negative Predictive Value.

egg white, Gal d 1 and Gal d 2 for each group-*UniCap-ThermoFisher Diagnostics®*. Statistical analysis with support of GraphPadPrisma7: t-student test; SPSS (v25): ROC curves.

Results: Were included 36 sera, 25 of egg-allergic patients, 11 egg-tolerant patients at the time of collection. Average age (years) of the Allergic Vs Tolerant: 5.8 Vs 8.1. There was a statistically significant difference between the group of Tolerant Vs Allergic for egg white sIgE ($P = 0.0006$) and Gal d2 ($P = 0.0004$), but without significance for Gal d 1 ($P = 0.055$). The values for sIgG4 and sIgE/sIgG4 were all statistically significant: sIgG4 from egg white ($P = 0.0122$), Gal d 1 ($P = 0.0294$) and Gal d2 ($P = 0.0387$) and ratio sIgE/sIgG4: egg white ($P < 0.0001$), Gal d 1 ($P = 0.0006$) and Gal d2 ($P = 0.0002$). Egg tolerance acquisition cut-offs were determined using ROC curves (Table 1).

Conclusion: Evaluation of sIgE, sIgG4 and sIgE/sIgG4 ratio for egg white and Gal d 2 can improve the diagnostic and follow-up of patients with egg allergy. Regarding Gal d 1, only the values of sIgG4 and sIgE/sIgG4 ratio were significative. *Cut-off* values were defined for all parameters, being sIgE/sIgG4 ratio the most reliable (>AUC).

TP1577 | Long-term clinical course of rush oral immunotherapy in patients with severe wheat and hen's egg allergy at a single center

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Background: It is said that desensitization can be expected as effects of oral immunotherapy. However, it is unknown how much stability will be achieved when rush oral immunotherapy (ROIT) is performed in a severe food allergy patients. The aim of this study is to evaluate the long term clinical course of ROIT in patients with severe wheat or hen's egg allergy in our hospital.

Method: ROIT is classified into build-up and maintenance phases. The maximum maintenance dose is 50 g of Udon dry noodles or 40 g of scrambled egg. During the maintenance phase, patients continue taking the maintenance dose regularly at home. Forty four wheat allergy patients and 41 egg allergy patients started ROIT from May 2011 to May 2015. Forty-one patients (men = 34) of the wheat ROIT group and 41 patients (men = 25) of the egg ROIT group who could be followed up for 3 or more years were included in this study. We retrospectively evaluated the proportion of patients with stable desensitization (SD). We defined SD clinically as being able to consume 50 g of Udon dry noodles or 40 g of scrambled eggs, being able to eat wheat or egg at weekly intervals, having no symptoms with exercise after intake, and being stable for more than 6 months without symptoms.

Results: The withdrawal rate during the build-up phase was 9.8% (N = 4) and 5% (N = 2) in the wheat and egg ROIT groups, respectively. The proportion of patients with SD in the wheat and egg ROIT groups was 12.2% (N = 5) and 32% (N = 13), respectively, after 2 years. After 3 years, this proportion increased to 17.1% (N = 7) and 49% (N = 20), respectively.

Conclusion: SD cases increased every year, but some patients still did not achieve this goal. Further studies are needed for patients with severe wheat and hen's egg allergy.

TP1578 | Long-term improvement of dietary life and burden after rush oral immunotherapy

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Background: The effect of oral immunotherapy (OIT) is promising, but the improvement of quality of life and the burden of the treatment are still debatable.

Method: In 2013-2014, we conducted rush OIT for 34 patients (age 5-12 years) with hen's egg, cow's milk or wheat allergies, which consisted of a 2-week rush phase in hospital, followed by a slow increase and maintenance phase. The patients and parents took part in an annual questionnaire survey for 3 years. The questionnaire consisted of 10 questions for patients and 18 questions for parents, asking about their anxiety in daily life and the burden of the treatment. The participants chose one of the following answers: 1: serious, 2: some, 3: uncertain, 4: a little, 5: not at all. Answers 1 and 2 were considered to reflect anxiety/burden.

Results: After 3 years of treatment, 18 patients achieved the free intake of the target food, but 16 patients still required a reduced dose or reduced physical exercise after intake. The parents' answers showed an overall improvement of the anxiety/burden in daily life, especially in anxiety about fatal accidents (94.1% to 29.4%). In contrast, 70.6% and 41.2% complained of a burden of treatment at 1 and 3 years, respectively. At 1 year, 67.6% of parents and 26.5% of patients feared an occurrence of allergic symptoms after the programmed food intake; this remained 32.4% and 26.5%, respectively, at 3 years. Fifty-six percent of the patients disliked consuming the target food at 1 year; this remained 44.1% at 3 years. A subgroup analysis revealed that patients with other food allergies (n = 16) and those who still required a reduced dose or a reduced amount of physical exercise failed to achieve an overall improvement in daily life.

Conclusion: Rush OIT provided an overall improvement of anxiety in daily life. However, the burden of intake persisted even after 3 years of treatment. Furthermore, the effect was limited to patients without other food allergies and to those who achieved the free intake of the target food.

TP1579 | Long-term outcome of oral immunotherapy for food allergy

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Background: Oral immunotherapy (OIT) has been extensively studied as a promising treatment approach in IgE-mediated food allergy (FA). However, it has not yet been recommended for routine clinical practice because of unknown long-term efficacy and safety.

Method: We performed a survey of OIT outcome in December 2017 to patients who undergone OIT as an experimental treatment for FA at our institution from December 2008 to October 2017. By using postcards or the website, daily intake of the allergenic food and induced symptoms by the intake were surveyed.

Results: A total of 242 patients were treated during the 10-year period and 159 of them (66%) replied to the survey. Percentages of the patients who did unlimited daily intake of the allergenic food were 47%, 21%, and 11% in those who had allergy to wheat, milk, and egg, respectively. Eleven patients (7%), 7 with milk allergy and 4 with wheat allergy, experienced severe induced symptoms that required emergency visits. Fatigue, exercise and mild infectious diseases were triggers of the adverse events. No fatality was reported.

Conclusion: Achievement rate of safe desensitization by OIT was not high, and risk of adverse reactions remained even after long-term treatment. Although there are patients who benefit from OIT, measures to predict and prevent adverse reactions must be established.

TP1580 | Impact of a food allergy educational training to improve food allergy knowledge and management in the university food services staff

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Background: Most of the anaphylactic reactions to foods occur in adolescents and young adults; therefore, it is essential that Universities learn how to deal with food allergy and prevent accidental exposure in the university food services. The aim of this study was to evaluate the impact of a food allergy educational training on knowledge of University food services staff'.

Method: A face to face training on food allergy was developed for the food services staff from the University of Porto. The training included general concepts about food allergy; epidemiology; clinical manifestations; prevention, diagnosis and treatment; food allergens labelling and avoidance; cross-contact prevention; emergencies; legal framework, and good work practices. A food allergy knowledge questionnaire to address the knowledge and management skills about food allergy was applied before and after the training. The questionnaire included 20 knowledge assessment questions about knowledge, practices and attitudes about food allergy. GLM - Repeated Measures was performed to analyse the improvement on the participants' knowledge.

Results: The study included a total of 64 participants, 84.4% female and 15.6 male. The mean age was 50.0 (10.1) years-old, and most (%) of the participants only finished the 9th grade of education. After the food allergy training the final mean (SD) score on the knowledge survey was significantly higher than the baseline for the University of Porto food services participants' [63.8 (16.6) % vs 54.6 (13.1) %; $P < 0.001$].

Conclusion: Food allergy training showed to be a good strategy to improve the knowledge of catering staff at the Universities' food services. Educational programs could be an important strategy to reduce accidental allergic reactions at the University Community, and to provide a safe and inclusive environment in public food services for students with food allergy.

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GASTROINTESTINAL IMMUNOLOGY AND EOE

TP1581 | Novel peripheral blood allergen stimulation test for non-IgE-mediated gastrointestinal food allergies in neonates and infants

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Background: The lymphocyte stimulation test (LST) considerably helps with the diagnosis of non-immunoglobulin E-mediated gastrointestinal (GI) food allergies. However, it poses several challenges, including the requirement of substantial amounts of fresh peripheral blood and lengthy culture times (~5-7 days). To overcome such challenges, we assessed changes in gene expression in peripheral blood mononuclear cells (PBMCs) after they were incubated with antigens for 24 hours instead of monitoring cell proliferation in LST. We found a correlation between a gene expression test and the conventional LST. We designated the gene expression test as the instant peripheral blood allergen stimulation test (iPAST). This study aimed to improve the iPAST to reduce required amounts of blood by using whole blood as the starting sample instead of PBMCs.

Method: Whole blood samples from GI cow's milk allergy patients and disease control children were stimulated with α-casein for 24 hours and subjected to genome-wide gene expression profiling analysis using microarray chips. The significantly up- or downregulated genes were selected as putative markers and further subjected to quantitative RT-PCR to confirm the changes in expression. The association to a conventional LST was assessed by receiver operating characteristic (ROC) curve analysis. Diagnostic accuracy of iPAST was also evaluated for GI food allergy patients and controls.

Results: Nine putative marker genes, including those known to be involved in allergic inflammation, such as *IL2RA* were selected and confirmed to express significant changes in expression upon allergen stimulation, specifically in the patient group. The areas under the ROC curve (AUC) of iPAST (*IL2RA*) with α-casein for positive LST and for the diagnosis of GI cow's milk allergy were 0.875 and 0.967, respectively.

Conclusion: We performed a novel allergen stimulating test (iPAST) using whole blood samples and found its diagnostic value for the conventional LST and the disease to be significant. The results suggest that using the iPAST with whole blood can be an alternative to the LST in diagnosing GI food allergies.

TP1582 | Altered intestinal permeability in patients with LTP allergy

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Background: The most common food allergy in Mediterranean adults is due to Lipid Transfer Proteins (LTPs). The spectrum of clinical manifestations is wide regarding organ involvement and severity. Gastrointestinal (GI) symptoms are frequent and not always directly related to LTP ingestion. The role of intestinal permeability in this condition has not yet been established. The objective of this study is to evaluate intestinal permeability, in patients with LTP allergy and persistent GI manifestations. Associated conditions influencing intestinal permeability, such as lactose, fructose and gluten intolerance and GI infections were investigated.

Method: Eight patients (100% female), median age 38 years (21-56), diagnosed with LTP allergy referring persistent GI symptoms were recruited. First, medical data collected included personal history of celiac disease and lactose and fructose intolerance. D-xylose breath test was performed by the administration of 25 mg of D-xylose, H_2 and CH_4 was measured in exhaled air every 30 min for 3 hours. Parasitological tests for *Giardia intestinalis* and *Blastocystis* sp. (PCR in feces), immunochromatography for *Helicobacter pylori* (feces) and IgA against *G. intestinalis* in saliva were evaluated.

Results: LTP specific IgE (positive > 0.35 kUA/L) ranged 0.53-100 kUA/L. Gastrointestinal manifestations included: dyspepsia, flatulence, diarrhea, constipation and gastro-esophageal reflux symptoms. Two patients had a personal history of celiac disease and one of lactose intolerance. Four patients (50%) presented an altered intestinal permeability study and 2 (25%) were non-conclusive. One patient showed a positive test for *H. pylori* (12.5%), two *G. intestinalis* (25%) in both PCR and IgA tests and four had a co-infection of *H. pylori* and *G. intestinalis* (50%).

Conclusion: Half of the LTP allergic patients with persistent GI manifestations evaluated presented intestinal permeability impairment. The majority of the patients showed a concomitant GI infection. Other conditions, such as food intolerances and autoimmune diseases, must be ruled out. The impairment of intestinal permeability may interfere the development of allergic sensitization and clinical manifestations after exposure to allergenic foods. Further studies are needed to define if altered intestinal permeability is the cause or consequence of food allergy.

TP1583 | Clinical course of patients with allergic proctocolitis and enterocolitis

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Background: Food allergy describes the reactions against foods that occur by means of IgE-mediated or non-IgE-mediated immunological mechanisms. Its prevalence varies between 2-8% in children. Although many laboratory examinations help in the diagnosis of food allergy, the benefits of examinations in patients presenting with non-IgE-induced proctocolitis or enterocolitis clinic are limited. In this study, we aimed to evaluate the laboratory and clinical features of patients with proctocolitis and enterocolitis in our clinic.

Method: The records of the patients who presented with bloody and / or mucus stool to the Dokuz Eylul University Pediatric Allergy Immunology Outpatient Clinic were reviewed retrospectively. Demographic characteristics, comorbid findings, laboratory results and clinical outcomes were obtained from chart reviews. Medical records of 75 children had been followed-up with proctocolitis or enterocolitis between January 2016-2017 were analyzed retrospectively.

Results: Among 75 patients, 35 (52%) were male. The median age at the time of diagnosis of patients was 3 months. Family history of atopy was determined in 43 (57.3%) patients. Sixty three (84%) and 12 (16%) of these patients were diagnosed with proctocolitis and enterocolitis, respectively.

In 64 patients (85%) patch test was negative and skin prick test was negative in 44 (59%) patients. With the medical history, clinical and laboratory investigations, 38 (50.7%) cow's milk allergy, 12 (16%) hen's egg allergy and 16 (21.3%) cow's milk and hen's egg allergy were determined.

Forty three (58.7%) of the patients had atopic dermatitis (AD). Although, all patients with hen's egg allergy had AD, 52.8% of patients with cow's milk allergy has AD ($P = 0.013$). While the median age of toleration of baked food was 12 [8.2-14] months, the median age of termination of elimination diet was 14 [12-20] months. There was no differences between patients with AD (12 [9-13.8] months) and without AD (12 [7-15]) in terms of toleration age of baked food ($P = 0.592$).

Food toleration age of patients with negative skin prick test (9 [7.5-12] month) was found to be lower than age of patients with positive skin prick test (13 [12-16] months) ($P = 0.02$).

Conclusion: We can conclude that skin prick test gives an idea about toleration age of food in patients with allergic proctocolitis and enterocolitis.

TP1584 | Frequency of allergy and congenital immunodeficiency in children with colonic lymph nodular hyperplasia

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Background: Lymphoid nodular hyperplasia (LNH) is common in young children but is not associated with clinical symptoms, and considered a physiological pattern event. In children with gastrointestinal symptoms and high density of lymphoid follicles could indicate pathological condition. The lumen of the gastrointestinal tract is continuously exposed to many food antigens and besides all of its other functions; the gut is a crucial site for the immunologic response. Association of LNH with different immune-mediated disorders, have led to the hypothesis that local immune regulation is involved in its pathogenesis. The aim of this study is to define the frequency of allergy and congenital immune deficiency in children with LNH.

Method: It is a descriptive-cross sectional study. Children with different clinical symptoms who underwent colonoscopy 2010-2017 at Tabriz children hospital were evaluated. Inclusion criteria was isolated LNH in colonoscopy report which done by one expert gastrointestinal subspecialist. Exclusion criteria were polyps, tumour and ulcers reported in colonoscopy, coagulopathy, infectious diarrhoea, secondary immune deficiency, inflammatory bowel disease, positive meckel scan. Finally we enrolled 52 patients, their information collected in compliance with ethics. The data were analysed using SPSS16 for descriptive statistics.

Results: LNH was observed in 113 of 303(37%) for whom colonoscopy had been indicated during a 7-year period. Finally 52 children enrolled 34 male (65%), 18 female (35%), with mean age of (5.25 + _3.2) that were referred for hematochezia (73%), chronic diarrhea (13%), abdominal pain (10%), constipation (2%) and anemia (2%). Hematochezia was the most frequent clinical presentation in these children. Personal history of allergy was presented in 19(36%) of patients and family history of allergy was presented in 14(27%) of patients, respectively. Pathology reported infiltration of mixed inflammatory cells in 30 of 50(60%) patients. The most frequency of allergy was reported in children with nonspecific changes at pathology report. Two cases of primary immune deficiency were defined.

Conclusion: The presence of LNH in symptomatic children at preschool age is common. Hematochezia is the most frequent clinical presentation. Based our study moderate frequency of allergy and two cases of immune deficiency was reported. This study cannot define the prognosis and the natural history of disease, but it is the first step to do more studies.

TP1585 | Eosinophilic esophagitis: Clinical manifestations, allergic sensitizations and outcomes

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Background: Describe clinical findings of patients with eosinophilic esophagitis (EoE) diagnosis, explaining endoscopic and histological characteristics, patterns of sensitization to food and the treatments used since diagnosis.

Method: We performed a retrospective observational study of our patients with EoE diagnosis at *Hospital Universitari de Bellvitge* (Barcelona) between 2009-2018. We described the results of skin prick tests to aeroallergens and food allergens, results of gastroscopies, esophageal biopsies and specific IgE determination regarding the results of skin prick tests.

Results: A total of 51 patients diagnosed with EoE were included in the study, of which 44 (86.3%) were men, with a mean age of 37.9 years old (range 18-71). 39 (76.5%) of them had history of atopic disease. Mean lag time between symptom onset and diagnosis was 7 years. All patients presented dysphagia, 20 (39.2%) had chest pain and 45 (88.2%) food impactions, of those 22.2% presented two or more episodes. Regarding the endoscopic findings, esophageal rings were observed in 34 (67.4%), an average of 46 eosinophils per high-power field in pathological anatomy. 36 (71%) patients had sensitization to food: 26% milk, 14% egg, 12% fish/seafood, 39% legumes, 16% wheat, 55% nuts, 47% fruits and 34% vegetables. 18 (35%) patients were studied for having specific IgE against rPru p3 (13 were higher than 0.1kU/L) and 7 patients were studied for having specific IgE against rPhl p12 (2 of them were higher than 0.1kU/L). 21 patients (41.2%) have been treated with proton pump inhibitor, 3 (5.9%) with topical corticosteroids, and 27 (52.9%) received both treatments. Among the 51 patients, 17.6% of them required esophageal dilatation.

Conclusion: There is a delay in diagnosis of eosinophilic esophagitis. Dysphagia was the most important symptom and many patients presented impaction. Most of them had sensitization to food, around 50% to nuts and fruits. Many patients required more than one drug to treat eosinophilic esophagitis. A fifth part of the subjects required esophageal dilatation.

TP1586 | Eosinophilic esophagitis, rhinitis and occupational asthma caused by cereal flour allergy

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Case report: A 37-year-old patient, diagnosed 10 years ago with rhinitis and occupational asthma related to cereal flour, prior to diagnosis having presented symptoms for 5 years. He worked at a bakery from the age of 20 until the age of 27; after changing his job, he remained asymptomatic. He tolerates cereal ingestion.

In 2015 the patient starts suffering dysphagia and undergoes episodes of impaction. Following treatment with PPIs, the histological study (2017) revealed 40 eosinophils per high power field, thus establishing a diagnosis of eosinophilic esophagitis.

Material: Prick-tests (SPT) were performed with aeroallergens (house dust mites, storage mites, fungi, dog and cat epithelium, and various kinds of pollen), wheat flour, barley, rye, oats, maize, rice and alpha-amylase,.

Specific IgE measurements (ImmunoCAP®) were determined against positive allergens in SPT and against omega-5-gliadin, alpha-gal and panallergens (LTP, PR10, profilin and polcalcin).

IgE-binding proteins were identified by means of SDS-PAGE and Immunoblotting, using as solid support cereal flour extract, spaghetti extract, and pizza dough extract, all of which both raw and cooked or baked.

Methods: SPT was positive to grass pollen, cereal flours (except for rice).

Specific IgE: (KU/L) Phl p 1 + 5b: 5.8, wheat 40.2, oatmeal: 3, barley 5, maize 0.65; for the rest of allergens < 0.1.

IgE-binding proteins were identified in cereal flours (14 KDa and 16 kDa) and in the raw spaghetti and pizza extracts (14-16 kDa) as well as in the cooked ones (40 KDa).

Results: The patient followed a cereal-free diet (with the exception of rice) for a period of six weeks, after which an endoscopy and a histological study were performed again yielding results inside the normal range. The patient avoids the ingestion of cereal, and is currently completely asymptomatic with no need for treatment.

Conclusion: In this patient an allergy to cereals seems to be the cause of his respiratory clinical history (via inhalation exposure) and of his eosinophilic esophagitis (via digestive exposure).

TP1587 | An eosinophilic esophagitis case mimicking cough variant asthma

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Case report

Background: Eosinophilic esophagitis (EoE) is a chronic, antigen-immune mediated inflammatory disease characterized by infiltration of eosinophils in the esophageal mucosa in the absence of other causes of eosinophilia. Patients may present at any age with varying symptoms. Clinical manifestations include vomiting, food refusal and growth retardation in infancy as well as GERD-like symptoms and dysphagia particularly in childhood and adolescence. Patients may be asymptomatic and incidentally be

diagnosed by upper endoscopy performed for other indications. Here we report a patient who presented to our outpatient clinic with cough variant asthma and eventually got the diagnosis of EoE histopathologically.

Case report: A six year-old male patient was admitted to the outpatient clinic with a complaint of occasional coughs that increase at nights and with effort for 3 years. Latest cough period have been around for 20 days. Due to his clinical reports from another hospital, he was given salbutamol treatment for his previous cough attack last year and had no apparent benefit. Although he did not describe any symptoms related to reflux, he was also put on empirical treatment of PPI which provided partial subjective benefit. He had no history of atopy. There was no allergic disease in his family. In our first visit, his physical examination was normal. No atopy detected in skin prick tests. Nebulized salbutamol therapy was given due to high frequency cough and asthma like cough pattern. Cough frequency decreased. He was put on inhaled corticosteroid therapy with the diagnosis of cough variant asthma. However, no obvious clinical response was seen with the high dose inhaled corticosteroid. High dose lansoprazole and antiacid therapies were added to exclude GERD. After 10 weeks, due to no clinical improvement, upper endoscopy was performed. The esophagus biopsy was compatible with eosinophilic esophagitis. Food prick and patch tests were performed but no food allergy was detected. Swallowed fluticasone propionate treatment was started and the patient was symptom free for 3 months.

Conclusion: EoE is an emerging disease with a complex and not completely understood pathogenesis. All physicians including pediatricians should be familiar with this clinical entity. If EoE is not diagnosed and untreated, remodeling of the esophagus will result in permanent organ damage. Our case is unique as cough is the only symptom in the diagnosis of EoE.

TP1588 | Eosinophilic esophagitis: A new component of the atopic march?

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Case Report:

Introduction: Eosinophilic esophagitis (EoE) is an immunologically mediated chronic inflammatory disease and shares pathophysiological and clinical features with other components of the Atopic March (AM)[1].

Case description: A 15-year-old teenager reported that he began feeling 'stuck' after meals two years ago. He presented morning sickness, especially after drinking cow's milk. The symptom disappeared spontaneously over time. He denied epigastric pain or sensation of gastroesophageal reflux. He had pruritus, nasal congestion and intermittent asthma attacks since the age of seven. He reported that he has always used soy milk because of allergy to cow's milk protein, diagnosed in the first year of life. Two years ago, cow milk and its derivatives were reintroduced in his diet. Clinical examination without alterations, skin prick test was strongly positive for aeroallergens and negative for extracts of cow's milk, egg, wheat, soybean, peanut and fish. Digestive endoscopy revealed thickened and white esophagus mucosa starting in the middle third with transverse and longitudinal stretch marks in the distal third. Appearance of the stomach and duodenum mucosa without alterations. Urease test: negative. Histopathological examination of the esophagus identified the presence of 22 eosinophils / field and epithelial hyperplasia.

Discussion: EoE is characterized by progressive esophageal dysfunction and can occur at any age. AM refers to the sequence of allergic diseases in childhood. A part of the atopics will classically evolve initially with atopic dermatitis (AD) and progress to food allergy mediated by immunoglobulin E, asthma and rhinitis. In a recent study of 449 patients with EoE, 46.1% had AD, 39% had asthma, 61.9% had allergic rhinitis and 21.6% had all three diseases. The treatment options for EoE are flexible and can be modified according to the needs, individual preferences, resources and evolutionary circumstances of the disease.

Conclusion: EoE, like other atopic conditions, presents different endotypes. However, it shares immunological and clinical mechanisms and is responsive to the control of allergens and corticosteroid therapy, like the other diseases of the Atopic March. Therefore, it is reasonable to assume that it can be considered a "fifth component", as presented in this case report, but further studies are needed to confirm these information.

TP1589 | A case of food-protein-induced enterocolitis syndrome (FPIES) with japanese clams and the lymphocyte proliferative response (LPR) with clam scratch test solution

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Background: FPIES with solid food is rare and LPR with a caused food may be useful to diagnose FPIES.

Method: Case presentation; A five-year-old girl showed severe abdominal pain, recurrent vomiting, and hypotension two hours after ingesting boiled Japanese clam (Asari). Rapid fluid infusion and intramuscular adrenaline injection were required. She had a history of similar reactions previously after Asari ingestions. Her Asari-specific IgE was < 0.1 UA/mL. Two years later, she had a challenge test with Asari. She ingested 0.5 g, 1 g and 2 g of boiled Asari in one hour intervals. Fifteen minutes after the third ingestion she developed fever, recurrent vomiting, headache and severe abdominal pain. Intravenous hydrocortisone injection and intramuscular adrenaline

injection were required. Her peripheral neutrophil count was doubled and C-reactive protein became positive.

To elucidate the effect of Lipopolysaccharide (LPS) contained in Asari, LPR tests with Asari meat and adjusted concentration of LPS solution were performed in three control adults and the patient. The LPR tests were performed with six different concentrations (3^0, 3^1, 3^2, 3^3, 3^4, and 3^5) of stimulation solution and data were shown in SI (stimulation index = mean H^3 cpm in cultures stimulated with testing solutions / mean H^3 cpm in unstimulated cultures). Next, to minimize the influence of LPS, we used Asari-scratch-test-solution (Asari extract) to stimulate lymphocytes in two control adults and the patient. Since the patient had opportunities, LPRs with the same lot of Asari extract were repeated three other days. These LPR tests were conducted by Bio Medical Laboratories (BML), Tokyo, Japan. The cytokine production profile of supernatant of LPR samples with Asari extract was also investigated by using the Luminex multiplex cytokine analysis kits and ELISA.

This study had been approved by the Ethics Committee of Yawatahama City General Hospital.

Results: The SI of LPR with LPS-containing Asari meat elevated even in adult control, just like LPR with adjusted LPS solution. On the other hand, SI of LPR with Asari extract elevated in the patient specifically and the results were reproducible. The maximum SI levels were 16.5, 18.9 and 27.5 in the patient and 3.2 and 3.4 in the control adults. Pro-inflammatory cytokines (TNF-a, IL-6, IL-1a, IL-1b), Th2 cytokines (IL-5, IL-13), IL-10, and GM-CSF were highly induced In the patient's culture supernatant.

Conclusion: LPR with Asari extract may be useful to diagnose FPIES with Asari.

TP1590 | Food protein induced enterocolitis syndrome (FPIES): A French cohort of 68 patients

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Background: FPIES is a potentially severe and probably underdiagnosed non-IgE-mediated food allergy. The aim of this study is to describe a large cohort of patients with FPIES from diagnosis to tolerance in order to provide elements to clarify their management.

Method: This is a retrospective observational study, describing the clinical and biological characteristics of the 68 children followed in the unit from January 1st, 2016 to December 31st, 2018.

Results: The median age at first allergic reaction was 5 months (0-25 months) with an age at diagnosis of 10 months (2.4 -37 months), after an average of 1.8 reactions. Fifty-two cases (74%) were diagnosed after 2 or more reactions. Allergy to cow's milk was the most common (n = 46, 68%). Eleven other foods were imputed, including eggs (n = 8, 12%), fish (n = 7, 10%), beef (n = 4, 6%) and rice (n = 3, 4%). Other allergens were apricots, avocados, raspberries, mushrooms, peanuts, apples and sheep. Nine percent of patients (n = 6) reacted to at least 2 groups of food. Specific IgE was found in 28% of patients (n = 19) without associated IgE-mediated reaction. The median age at first oral food challenge (OFC) was 19 months (4 months-7 years). On 114 OFC, intravenous rehydration was required in 13% of cases (n = 15), and fluid resuscitation once. Forty-five children are currently cured, with a median age of healing at 2 years (8-42 months) after an average of 2 OFCs.

Conclusion: FPIES is probably more frequent than it appears because the diagnosis is made in only a quarter of cases after the first reaction. One-third of the patients also had IgE sensitization. The reintroduction modalities are still unclear despite the international consensus of 2017, and the physiopathology remains to be clarified in order to avoid potentially dangerous OFCs.

TP1591 | The diagnostic value of in vitro food allergen-specific IgE in children with clinical history of food-induced allergic symptoms

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Background: Food allergy become common in children and adults in recent years. Clinical history with positive skin prick tests or food-specific IgE help us to make diagnosis precisely. Comparing to skin prick test, food-specific IgE is a more safe and rapid test in outpatient department. Our goal is to evaluate how reliable of food-specific IgE in the diagnostic of food allergy.

Method: We collected total 16 patients (mean age = 3.3; gender ratio (M:F) = 11:5), who presented clinical food allergy history, by questionnaire and medical records from 2013-2018. Blood sample was sent for further evaluation of allergen-specific IgE (BioIC). We divided these patients into four groups (egg, milk, peanut and shellfish) of food allergy and analyzed the positive predictive value and negative predictive value.

Results: For these patients, we found that the best positive predictive value (PPV) were milk (PPV = 0.8, NPV = 0.82) and peanuts (PPV = 0.80; NPV = 0.82) and negative predictive value (NPV) was shellfish (PPV = 0.33; NPV = 0.92), followed by egg allergy (PPV = 0.56; NPV = 0.86)

Conclusion: For food-specific IgE, positive findings of milk and peanut allergens sensitization seemed more comparable to clinical history. On the other hand, negative finding of shellfish allergen has higher chance to exclude shellfish allergy. However, due to low numbers of patients, more case data are needed for further confirmation.

TP1592 | Description of 1002 oral food challenges performed in a pediatric allergy unit

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Background: Oral food challenges (OFCs) are the gold standard for food allergy (FA) diagnosis. We aimed to describe the frequency of the most common foods requiring an OFC to clarify the FA diagnosis, the patient′s clinical features or the tolerance to specific food.

Method: A retrospective observational study was performed in October 2018 for patients recruited between January and October 2018 (0-18 y.o.) with suspected IgE-mediated FA who underwent an open OFC. Presence of asthma, skin prick test (SPT) and specific-IgE values to the culprit food were evaluated. OFCs were considered positive when objective symptoms or subjective persistent symptoms appeared. Food portions were adjusted according to the patient′s age. Adverse events (AE) during OFCs were classified according to the organ affected and anaphylaxis was defined according to the EAACI Anaphylaxis Guidelines.

Results: We performed 1002 OFCs on 685 children, where 133 (13%) were positive. The average age was 7 years and 6 months (range 1 month-18 years). 359 (36%) OFCs subjects presented asthma as a baseline disease and 423 (62%) were male. 638 (64%) of all OFCs showed sensitization to the involved food, either by a positive SPT or specific-IgE. Among positive OFCs, SPTs were positive in 119 (89%) and specific-IgE in 65 (49%). Egg was the most frequent food challenged with 204 (20%) OFCs (raw egg 13% and boiled egg 7%) followed by cow′s milk 89 (9%). Other OFCs included any nuts 309 (31%), fish 175 (17%), legumes 74 (7%), fruits 71 (7%), and other foods 80 (8%). The most common AE was cutaneous (erythema, local and generalized urticaria) in 80 (60%) positive OFCs followed by respiratory symptoms (hydrorrhea, sneezing, mild and moderate airway obstruction) in 67 (50%). The most frequent AE symptom was hydrorrhea (36%) followed by local urticaria (35%) and sneezing (30%). When categorized by food, egg was associated with hydrorrhea (50%) and cow′s milk with sneezing (44%). Among positive OFCs, one organ system was affected in 61% and two or more in 39%. 20% presented anaphylaxis, and all responded well to treatment, with no serious adverse reactions.

Conclusion: The most frequent food challenged was egg followed by cow′s milk. The majority of OFCs performed had a negative outcome and cutaneous symptoms were the most common AE. 20% of positive OFCs presented anaphylaxis as an AE and no serious adverse reactions were observed, supporting the idea that OFCs are a safe diagnostic procedure when performed by highly specialized personnel.

TP1593 | Wheat-dependent anaphylaxis induced by exercise and stress. Case report

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Background: Food-dependent exercise-induced anaphylaxis (FDEIA) is a subtype of exercise-induced anaphylaxis (EIA), which is characterized by the onset of anaphylaxis during or shortly after a physical exercise in response to ingestion of a causal food allergen. Wheat is one of the staple foods in the diet of Ukrainians. Wheat can cause allergic rhinitis and food allergies. In addition, wheat allergies can induce various symptoms such as the atopic dermatitis, urticaria, and wheat-dependent exercise-induced anaphylaxis (WDEIA). WDEIA is a rare, but potentially severe food allergy exclusively occurring when wheat ingestion is accompanied by such cofactors as exercise or stress. Here we report two our clinical cases of WDEIA.

Method: Here we report two our clinical cases of WDEIA.

Results: A 36-year-old man was presented with urticaria which was developing 20 minutes after intensive training in the swimming pool. He did not associate his symptoms with any food. Physical examination and general blood test did not reveal any abnormalities. Skin prick test (SPT) and specific IgE assay to the most common food allergens were negative. ImmunoCap molecular test revealed sensitivity to W-5-gliadin (rTri a 19,) 6.13 kU/L (wheat component). Further testing with advanced component diagnostics ISAC confirmed that sensitization presented only to rTri a 19 (7.2 ISU/L). We performed the exercise provocation test and discovered the presence of food challenge to wheat. A 44-year-old man was presented to having recurrent anaphylaxis of unknown cause. His symptoms started in 2017 and occurred 3 times a year, in a form of severe edema of the lip and the eyelids, accompanied by generalized urticaria and a drop in blood pressure. Symptoms usually developed in stressful situations after consumption of foods containing wheat (pancakes, sandwiches etc.). In the absence of stress factors the symptoms described above were not observed. SPT was negative to all tested food and inhalant allergens. ImmunoCap analysis revealed elevated levels of IgE specific to W-5-gliadin (rTri a 19,) 4.64 kU/L.

Conclusion: In case 1, anaphylaxis in response to wheat consumption was induced by the exercise, while in case 2 it was induced by the stress. Both patients were diagnosed with wheat-dependent exercise-induced anaphylaxis (WDEIA). They were advised to eliminate wheat before exercise and in stressful situation and carry an adrenaline auto-injector (Epi-Pen) with them at all times for emergency.

TP1594 | Asymptomatic sensitization to nuts in children with eczema: Estimation of risk of clinical reactivity

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Background: Estimation of risk of clinical reactivity to nuts with asymptomatic sensitization of children with eczema or other food allergies.

Method: Retrospective study of children aged 5 months- 15-years-, with a history of IgE reaction to foods and/or eczema. Skin prick tests (SPTs) were performed to all nuts implicated to the reaction or had not been consumed. Data recorded included: personal history of atopy, maximum diameter of SPT/prick to prick, specific IgE and oral food challenge (OFC) outcome to nuts.

Results: 72 children (31.9%) (mean age of 5.5 ± 3.4 years,18 males) were included and 23 had positive SPT to nuts, (11 / 23 children had LPT sensitization). Reactions to foods were as follows: Cow's milk = 9, egg = 9 (5 had to both CM and egg) 9, sesame = 2, and 3 to other foods. All children had positive history of atopic dermatitis, 52.17% allergic rhinitis and 39.13% asthma. 47 OFC were conducted. 2/ 47 OFC (4.25%) were positive: one/eleven to hazelnut (f17: 12.3 ± 17.7KU/L. SPT: 4.39 ± 4.24 mm, P2P: 5.23 ± 7.15 mm) and one /eight to walnut (f256: 11.6 ± 17.05KU/L, SPT 4.5 ± 1.2 mm, P2P: 3.88 ± 1.78 mm). All other were negative: 11 to peanuts (f13 = 1.9 ± 0.84KU/L, SPT: 3.3 ± 2.38 mm, P2P: 1.7 ± 2.28 mm), to pistachios (f203: 1.05 ± 0.45KU/L, P2P: 4 ± 4 mm), 3 to cashews (f202: 2.87 ± 2.66KU/L,P2P: 7.8 ± 6.03 mm) and 12 to almonds (f20: 4.28 ± 4.99KU/L, SPT:3.72 ± 2.44 mm, P2P: 3.4 ± 2.47 mm).

Conclusion: Patients with positive reaction to nuts often avoid all nuts, nevertheless the risk of clinical reactivity is rather low in our population.

It is essential for children with eczema or food allergy to be tested for nuts, as a high percentage of sensitization is recorded (31.9%). Nevertheless, the risk of clinical reactivity is low.

TP1595 | Evaluation of correlation between LTP's sensitization patterns and severity of anaphylaxis

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Background: LTP's are the main elicitors of food allergy in Spanish Mediterranean shore and there is a high cross-reactivity among

	Pru p 3	Cor a 8	Art v 3	Pla a 3	Jug r 3	Tri a 14	Ole e 7	Ara h 9	Par j 2	
511	1X	1	1	1	1	1	1	1	1	1
503	1	1	1	1	1	0	1	1	1	1
510	1	1	1	1	1	1	1	1	0	6
502	1	1	1	1	1	0	1	1	0	5
506	1	1	1	1	1	1	0	1	0	3
498	1	1	1	1	1	0	0	1	0	15
496	1	1	1	1	1	0	0	0	0	4
370	1	0	1	1	1	0	0	1	0	2
434	1	1	0	1	1	0	0	1	0	2
433	1	1	0	1	1	0	0	0	1	1
368	1	0	1	1	1	0	0	0	0	1
432	1	1	0	1	1	0	0	0	0	3
278	1	0	0	0	1	0	1	1	0	1
418	1	1	0	1	0	0	0	1	0	1
400	1	1	0	0	1	0	0	0	0	1
336	1	0	1	0	1	0	0	0	0	1
304	1	0	0	1	1	0	0	0	0	3
386	1	1	0	0	0	0	0	1	0	1
274	1	0	0	0	1	0	0	1	0	1
290	1	0	0	1	0	0	0	1	0	1
257	1	0	0	0	0	0	0	0	1	1
										55

them. However, correlation between grade of anaphylaxis and LTP sensitization patterns has not been described.

Method: 210 patients (both gender, older than 14 y.) attended at Allergy Department were included. Serum tests were performed by ImmunoCAP© ISAC 112 (Phadia AB, Uppsala, Suecia). Results > 0.35 ISU to LTP's were considered positive. LTP's patterns were determinate by combination of the 9 LTP present in ISAC® and nominated according to Allergen Profile Codification System (APCS). Anaphylaxis severity degree was established based on two categories: Type A (Müller grade I-II) and Type B (Müller III-IV). Contrast hypothesis testing was performed to evaluate correlation between LTP pattern and anaphylaxis severity.

Results: 160 patients (76.5%) showed type A anaphylaxis and 50 (23.5%) type B. Four LTP's profiles were described regarding to higher level of sensitization to an specific LTP component: peach profile (PP) in 46% of patients, walnut profile (WP) in 37.22%, peanut profile (PeP) in 5.11% and hazelnut profile (HP) in 2.91%. Twenty-one different patterns have been described in PP, 16 in WP, 6 in PeP and 3 in Cor a 8. None single LTP showed correlation with severity. Pattern 510 (APCS) in PP was correlated with type B anaphylaxis ($P < 0.05$).

Conclusion: In our patients with LTP food related allergy the most common type of anaphylaxis is mild-moderate. Single LTP's tested have no showed correlation with severity. Only one LTP combination (510 pattern) showed correlation with severity. These findings could play an important role in clinical management of these patients.

TP1598 | Gluten fermentation with selected lactic acid bacteria strains induces its proteolysis and decreases its antigenicity

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Background: The nutritional and functional properties of a product can be improved by the fermentation process. It is an interesting area of research which entails the ability to hydrolyze allergenic proteins of the food into smaller peptides. In this work, we try to assess the capacity of lactic acid bacteria isolated from fermented foods to hydrolyze the gliadin fractions which are responsible for wheat allergy.

Method: Lactic acid bacteria (LAB) strains isolated from sourdough, fermented milk and other fermented foods were screened for their proteolytic activity using a specific gluten medium. The 48 h old MRS broth culture of these strains was inoculated into a solid gluten medium for 24 h before being re-inoculated at 10% into specific gluten enriched medium and incubated in anaerobic condition during 24 h at 30°C. Total gliadins fractions were extracted from each fermented products and analyzed by SDS-PAGE and RP-HPLC to check the strain's proteolytic activity. The proteolysis products of gliadins after fermentation were examined using specific polyclonal antibodies directed against repetitive domains of gliadins by Dot blot and western blot.

Results: Among 200 strains screened, 09 exhibited high proteolytic activity with a maximum degradation of gliadins as demonstrated by SDS-PAGE and RP-HPLC pattern. No alpha-gliadins IgG immunoreactivity was detected in the fermented gluten obtained by four proteolytic LAB strains.

Western blot pattern showed also that hydrolysis products in the fermented gluten reacted neither with N-ter specific IgG antibodies nor with specific IgG to repetitive domains. These results suggest that the proteolytic activity of lactic acid bacteria could proteolyze the N-ter domain and the repetitive domain of these proteins. The degradation of the repetitive domain is promising for limiting allergenicity as it contains potential IgE epitopes involved in wheat allergy. The eliciting phase of allergy by using basophile degranulation test will be performed to explore the residual allergenicity of the fermented gluten products.

Conclusion: The studied strains with their distinct proteolytic activity may be a well-adapted tool for the reduction of gluten allergenicity and could represent a good ingredient to produce hypoallergenic gluten-based products.

TP1599 | Effect of the specific IgE level on the eliciting dose in patients with cow's milk allergy evaluated by a positive oral food challenge

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Background: Predicting the eliciting dose (ED) by conducting an oral food challenge (OFC) is beneficial to patients with food allergy, as it helps avoid risks, such as severe anaphylaxis or lethal allergic reactions. Although specific IgE levels have been regarded useful to determine the probability of positive diagnosis during OFCs, there are limited studies on predicting the ED using specific IgE.

Method: Patients who were confirmed positive for milk allergy in an open milk challenge (based on the presence of objective symptoms) at the National Centre for Child Health and Development between the year 2015 and 2017 were enrolled. The OFCs were conducted at 40-minute intervals using a three graded dosing method. Interval-censoring survival analysis, the log-normal, and Weibull distribution models were used to estimate the threshold dose distribution and EDs. Moreover, stratification analysis using milk specific-IgE class (ImmunoCAP) was performed.

Results: Overall, 388 patients participated in the OFC; patients' median age was 5 years (range, 0–15 years of age; 67% male). Patients with CAP class 2 accounted for 15%; class 3, 35%; class 4, 23%; class 5–6, 25%. The distribution curves for the objective eliciting threshold were determined. The ED_{50} of CAP class 2 group was 181 mg milk protein (95% CI: 122–268); class 3, 115 mg (86.9–152); class 4, 59.8 mg (43.1–83.0); class 5–6, 59.8 mg (43.1–83.0). In patients with severe milk allergies (CAP class 5–6), ED_{05} was 1.23 mg (0.79–1.92), and the lowest observed adverse effect level (LOAEL, ED_{01}) of milk was calculated to be 0.475 mg (0.014 mL).

Conclusion: This study suggested that there was a relationship between the specific IgE level and eliciting dose. Further studies are required to establish a safer challenge testing method.

TP1600 | Sensitization to molds through the digestive tract: A case report

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Case report: Manifestations of mold allergy are classically related to symptoms of asthma and other respiratory diseases; however, there have been reported a few cases of food allergy to molds after ingestion of fermented food. It is a common practice to add flavour-enhancing molds to traditional foods, for example dry fermented sausage. We report the case of a 25-year-old woman diagnosed with rhinoconjunctivitis and asthma due to allergy to pollens. In the past year she had experienced an episode of facial angioedema and urticaria immediately upon ingestion of a few slices of dry fermented sausage, which she had tolerated previously on many occasions. The symptoms subsided spontaneously in under 6 hours. She tolerated all other types of meat products.

Method: We perform the following tests:

1) Skin prick test to pneumoallergens (included alternaria tenuis, aspergillus fumigatus, cladosporium herbarum)

2) Prick by prick to dry fermented sausage

3) Total serum IgE and specific IgE determinations of Penicillium chrysogenum, Alternaria alternata, Aspergillus fumigatus, Aspergillus niger, Candida albicans and Cladosporium herbarum

4) Oral challenge test.

Results: The skin prick test was positive for cypress and olive pollen and negative for molds tested. Prick by prick to dry fermented sausage was positive with skin and flesh. Total serum IgE was 184 UI/mL and specific IgE determinations was positive for Penicillium chrysogenum (1.29 UIa/mL) and negative for the others molds. The oral challenge test was positive. The diagnosis was facial angioedema and urticaria after dry fermented sausage due to IgE-mediated allergy to Penicillium.

Conclusions: - We demonstrated that IgE-mediated hypersensitivity to Penicillium chrysogenum was responsible for the patient's reaction and consider that primary sensitization probably occurred by the oral route.

- In that type of patients, we should recommend avoiding all products commonly contaminated with molds such as dry fermented sausages, Spanish ham, foie gras and French fermented cheeses.

TP1601 | Profile of 15 patients with food dependent exercise induced anaphylaxis from India

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Background: Anaphylaxis is a serious form of IgE mediated allergic reaction. Food dependant exercise induced anaphylaxis (FDEIA) is a distinct and rare cause of food induced anaphylaxis. It is characterised by onset of symptoms of anaphylaxis following exercise within 4 hours of suspected food intake. It is usually missed and delays in diagnosis are present with considerable morbidity and mortality. We report the profile of patients diagnosed with FDEIA at an allergy centre from South India.

Method: This is a retrospective review of patients diagnosed at a tertiary care allergy centre from Chennai, India between 2016-18. FDEIA was diagnosed as per WAO guidelines for anaphylaxis fulfilling criteria for FDEIA. Case records were analysed including clinical history, results of skin prick testing and invitro testing and Oral Food and exercise challenge testing were done where appropriate.

Results: A total of 13 patients were diagnosed with FDEIA during this period (Males = 7, Females = 6) with mean age 20.4 years. Gluten was the implicated food in 9 patients while chick pea (1), Coconut (1), shrimp (1) and Kidney Bean (1) were the other, which was confirmed by SPT (n = 13), ImmunoCAP (n = 7) oral food challenge testing (n = 5) and omega-5 gliadin (n = 2). Food and Exercise challenge was positive in 5/5 patients tested. All patients (13/13) presented with Urticaria, 12/13 had Angioedema, 12/13 with respiratory symptoms, 3/13 had GI symptoms and 5/13 presented with shock. All patients reported at least 2 episodes of anaphylaxis. Mean Time to onset of Anaphylaxis after Food intake with exercise was 23 mins. All patients showed aeroallergen sensitisation. All patients had respiratory allergies (Allergic Rhinitis, Bronchial Asthma)

Conclusion: Gluten was found to be the most common etiological agent associated with FDEIA. Hence, a detailed clinical history and extensive evaluation including Food and Exercise challenge testing should be done. Gluten should be considered in all cases of unexplained anaphylaxis.

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CASE REPORTS IN FOOD ALLERGY AND FOOD-INDUCED ANAPHYLAXIS

TP1602 | A case of systemic allergy to quorn

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Case report: Quorn is a brand name for a mycoprotein food commonly used as a meat substitute in vegetarian meals and produced from the mould *Fusarium venenatum*. We report a case of systemic IgE-mediated symptoms after ingestion of Quorn.

A 35-year-old female vegan patient developed a pruritic erythematous maculopapular rash consistent with urticaria over the chest and abdomen within a few minutes of eating a meal containing Quorn, nutritional yeast and rice. She subsequently developed tightness of the chest and shortness of breath. She was reviewed by paramedics and treated with intravenous antihistamines before being taken to Accident and Emergency. Observations including blood pressure and oxygen saturation were normal and remained stable. Her symptoms resolved without any need for further treatment. In the Allergy clinic, prick-prick testing with Quorn was strongly positive with the development of a 10 × 5 mm wheal. (Histamine positive control 5 × 5 mm, negative control 0 mm). The patient developed pruritus during skin testing and was treated with oral antihistamine. Subsequent additional skin prick testing to *Alternaria alternata* was 2 × 2 mm and *Cladosporium herbarum* 0 × 0 mm. Specific IgE testing to Yeast was negative. The patient was advised to avoid all Quorn containing products and trained to self-treat acute allergic reactions with antihistamine and self-administered adrenaline.

IgE-mediated reactions to Quorn are uncommon but have been reported (Hoff et al. JACI 2003). *Fusarium venenatum* cross reacts with other moulds including *Aspergillus fumigatus*, *Cladosporium herbarum* and *Alternaria alternata*. Patients sensitised to these environmental moulds via the respiratory tract may subsequently develop hypersensitivity following ingestion of Quorn (Tee et al. Clin Exp Allergy 1993). The negative skin test to moulds could be a false negative as it was preformed after she was treated with antihistamine. Systemic IgE-mediated hypersensitivity reactions to mycoprotein (Quorn) are rare but clinically significant, especially in patients with inhalant mould allergy.

TP1603 | Food allergy to cassava without latex sensitization

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Case report

Background: Cassava is a frequently consumed food in the world. Despite its high consumption, only a few cases of food allergies to cassava are described in the literature. These cases are mostly described in association with latex allergies, in particular via the rHev b5 protein. We describe here a case of true food allergy to cassava, without associated latex sensitization but with demonstration of associated sensitization to LTP.

Method: A 23-year-old woman coming from Madagascar came in consultation with a story of three episodes of urticaria with angioedema and hypotension after several meals containing cassava ("Ravitoto"), and other foods like rice, mango, peanut, beer, coconut milk. Each time it happened in a menstrual period in association with intake of ibuprofen for the first two episodes.

Results: 1. Skin test (Stallergenes°) were positive for birch, wormwood, soy, wheat, nut, walnut peanut, negative for latex

2. Native skin tests were positive for litchie, mango, kiwi, peanut, and negative for coconut.

They were positive for raw manioc leaves at 10 × 20 mm, cooked at 5 × 5 mm, raw root at 5 × 5 mm, negative for cooked tuber

3.Immunocap (Thermofisher°) was negative for r Bet v1-v2-v4, -r Ara h2-h3, latex and available recombinants (r Hev b1-3-5-6.01-6.02-8-9), positive for r Cor a 8 at 36.4 Ku/L, r Ara h9 at 20.3 kU/L. Immunocap was not available for cassava

4.The oral provocation test was positive for cooked cassava leaves at the cumulative dose of 80 g. The patient presented significative urticaria and angioedema.

5.Clinical evolution was good after evicting cassava. The patient is going on with consuming a lot of LTP foods without associated symptoms

Conclusion: This patient has a confirmed allergy to cassava leaves. This case, contrary to the cases previously described in the literature, is without associated sensitization for latex. The patient has associated sensitization to LTPs that seems to be asymptomatic, but the potential role of LTP in her cassava allergy can't be ruled out. Taking anti-inflammatory drugs (and menstruation?) may have played a role of co-factor. It would be interesting to complete the exploration by inhibition test with LTP and cassava leaves.

TP1604 | Occupational allergy to barnacle

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Case report

Background: Barnacles *(Pollicipes pollicipes)* are a seafood type belonging to the *Scalpellidae* family, which are located in warm water shores and are known to be consumed in the Iberian Peninsula, France and South America. Barnacle allergies are not frequently

reported and there is very little publication on the subject. However, there have been cases of sensitization by the digestive tract and also by cross-reactivity with mites.

Case Report: A 57-year-old man presented with naso-ocular itching, sneezing, rhinorrhea, lacrimation, palpebral and facial angioedema and pruritic wheals at contact areas with barnacles. He has worked in the hospitality industry for five years and has a history of moderate persistent seasonal allergic rhinoconjunctivitis and pollen-induced asthma. He has reported that his symptoms started three years ago after handling barnacles and having exposure to cooking fumes. He reports never having ingested barnacles and he tolerates digestion of other crustaceans, bivalves and cephalopods both raw and cooked.

Methods and results: Prick tests were carried out with commercial extracts of aeroallergens, anisakis, tropomyosin, mussel, oyster, clam and prawn, prick by prick with barnacles (raw and cooked) and prawn (raw and cooked) and specific IgE determination for prawn and mussels. Skin tests (prick test) were positive for grass, olive tree and anisakis and negative for moulds, mites, tropomyosin, danders, mussel, oyster, clam and shrimp. Prick by prick with raw barnacles and cooked barnacles were positive and negative for prawn (raw and cooked).

In vitro study: total IgE was 386 kU/L with specific IgE to anisakis of 19.9 kU/L, and negative to prawn and mussel.

Conclusion: We present a case of occupational rhinoconjunctivitis and contact urticaria/angioedema due to IgE-mediated allergy to barnacles. In our patient, sensitization to barnacles was not digestive but cutaneous and/or by inhalation without cross reactivity with mites. Based on the reviewed literature, this would be the first case of sensitization to barnacles in an occupational setting.

TP1605 | Serious coconut allergy in thai patient: Induction of oral tolerance

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Background: Allergy to coconut (tropical fruit that is obtained from the coconut tree (*Cocos nucifera)*) is a very rare entity. Currently the only valid therapeutic alternative in food allergy is the restrictive diet. Our goal is to offer a treatment option through a desensitization guideline.

Method: *Clinical case*: 47-year-old patient, from Thailand, with a history of moderate mite rhinoconjunctivitis treated with specific immunotherapy with good response, was diagnosed of ANAPHYLAXIS BY COCONUT after presenting pharyngeal itching, dysphonia and immediate palmar itching with the intake of coconut in any amount and /or presentation. A strict avoidance diet is recommended.

Complementary tests: *Positive* skin prick-test to coconut and coconut milk. *Positive* prick-prick to coconut. *Positive* rubbing-test (++). Total IgE 296.70 UI/mL. Coconut-specific IgE 17.70 kUI/L. No oral provocation test was performed because she had an episode of anaphylaxis after rubbing-test.

Method: For cultural reasons, the coconut is very consumed in her family environment, so the risk of accidental intakes is very high. It was decided to carry out a desensitization protocol, which consists of administering increasing doses of coconut milk in different dilutions (1/100, 1/10) until reaching a total dose of 6 g of grated coconut a day. The procedure lasts 4 weeks and during the same, the patient presents mild reactions that cease without treatment, except on one occasion that required desloratadine 5 mg orally.

Results: - The patient has completed the protocol without significant adverse events.

- Currently in the maintenance phase (6 g/3-4 times per week) with good tolerance after a year and a half of having completed the desensitization protocol. Despite a non-strict adherence to the maintenance dose, the patient performed a free diet including coconut and had no further reactions.

Conclusion: - Oral desensitization can be a safe alternative in patients with coconut allergy.

- More experience is needed to assess their safety, like so their impact on the evolution of food sensitization.

TP1606 | Banana hypersensitivity in Thailand: Case series

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Background: Banana has been recognized as one of important food allergen sources. Nowadays banana hypersensitivity has been reported more frequently with various presentations from oral allergy syndrome to anaphylaxis. This study aims to describe the pattern of banana hypersensitivity and the diagnostic test.

Method: A retrospective study of banana hypersensitivity at Ramathibodi hospital from 2015 to 2018.

Results: Six patients with the immediate hypersensitivity reaction to the banana were recruited. Four of them (66.67%) experienced multiple episodes of banana anaphylaxis, and two patients had oral allergy syndrome. Regarding to the diagnostic investigation, prick to prick skin test had higher sensitivity and specificity than the commercial banana extract and the concordance with specific IgE banana was reported. The cross-reactivity between the species of banana, kiwi, the avocado was documented in all patients. Latex skin prick test and application test were applied with negative results.

From the oral food challenge test, one of banana anaphylaxis patient can tolerate heated banana, while one who presented with oral allergy syndrome reacted baked banana.

Conclusion: The various phenotypes of banana hypersensitivity were identified. The prick to prick test is valuable for diagnosis of banana hypersensitivity. However, CRD might be needed for conclusive diagnosis.

TP1607 | Anaphylaxis due to mango and lychee in a patient sensitized to artemisia vulgaris

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Background: There is little evidence in the medical literature about the allergy to lychee (*Litchi chinensis*), a tropical fruit native to southern China. Cases of anaphylaxis have been reported in patients sensitized to mugwort and latex. A case of allergy to lychee and mango in a patient sensitized to mugwort is described.

Method: Male patient of 50 years, farmer in plantation of mangoes, with a history of diabetes mellitus and celiac disease. He was initially studied for two episodes of facial swelling and dyspnea after possible mango intake. Its implication was confirmed after positive oral provocation test.

He remained asymptomatic for three years with a diet free of mango and tolerance to other fruits. He continued working on a mango farm. He is studied again for generalized urticaria and intense rhinoconjunctivitis after intake of fresh lychee; he had not eaten it previously.

Results: *In vivo* study:

- Prick-test to common pneumoallergens in our environment: *positive* mugwort pollen.
- Prick-test to mango: *negative*.
- Prick-test to latex: *negative*.
- Prick-prick to mango: *negative*. Rubbing-test mango: *negative*.
- Prick-Prick to fresh lychee: *positive* for pulp, *negative* for skin and bone.
- Test of oral exposure to mango: presented intense rhinoconjunctival symptoms after 10 minutes of the intake of 10 g of mango.

In vitro study:

- Mugwort-specific IgE 2.69 kUI/L.
- Mango-specific IgE 0.19 kUI/L.
- rPru p3; Peach (LTP) < 0.10 kUI/L.
- ISAC (Immuno Solid-phase Allergen Chip): latex components < 0.3 ISU-E; only *positive* for mugwort defensin (Art v 1).

Conclusion: Mango and lychee share taxonomic characteristics; both belong to the phylogenetic division *Magnoliophyta*, as *Artemisia vulgaris*, although they are framed in different families.

Art v 1 allergen may be responsible for cross-reactivity between mugwort and mango, as well as other fruits.

It is suggested that sensitization to mugwort could also be responsible for the possible cross-reactivity of our case.

New studies are required for a better knowledge of mango and lychee allergens, as well as their possible cross-reactivity.

TP1608 | Edible insects: Investigation of cross-reactivity and reduction of allergenicity

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Background: Insects have become increasingly interesting as alternative nutrient source for human food and animal feed. Some safety aspects need to be addressed first, among them allergenicity. We investigated the *in vitro* cross-reactivity of shrimp-, mite- and flies-allergic patients to different edible insects. Furthermore, we assessed the efficacy of food processing in reducing the IgE-recognition of insect proteins and the allergenicity in skin prick tests (SPT).

Method: IgE from patients allergic to crustaceans, house dust mite (HDM) and/or stable flies was evaluated for cross-recognition of proteins in house cricket *Acheta domesticus* (AD), desert locust *Schistocerca gregaria* (SG) and Yellow mealworm *Tenebrio molitor* (TM). For food processing, different extraction methods, enzymatic hydrolysis, and thermal processing were applied for migratory locust (*Locusta migratoria*, LM).

Results: IgE from patients with crustacean-allergy shows cross-recognition of AD, SG and stable flies; house dust mite allergics' IgE binds to AD and SG; and the flies-allergic patient recognized cricket, desert locust and migratory locust. Cross-reactivity and most importantly also SPT-reactivity to LM could be deleted by conventional food processing steps, such as hydrolysis with different enzymes or autoclaving.

Conclusion: This study evidences that for edible insects appropriate food-processing methods can be applied to reduce the risk of cross-recognition by IgE and allergenicity in SPT in crustacean- and HDM-allergic patients. Supported by grants of the Austrian Science Fund FWF to EJJ (SFB F4606- B28 and MCCA DK W 1248-B13) and by the Austrian Research Promotion Agency FFG to IPS („Talente entdecken/Discover talents" 7121459-3 + 4).

TP1609 | What regulatory framework governs food allergy management in Lebanon?

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Background: Food allergy (FA) ranges in severity and can be fatal when anaphylaxis occurs. So far there is no curative treatment for

FA; its management relies on avoidance diets and treating accidental exposures when occurred. Food allergen labeling is necessary to help patients successfully meet their avoidance diet plans. Allergen labeling is governed by regulations. The aim of this article is to investigate FA management in Lebanon from its regulatory perspective.

Method: An extensive literature review of regulations and standards related to FA or food allergen labeling was carried out; followed by investigating national regulatory guidelines for the management of FA in Lebanon. The list of legal provisions adopted to monitor food institutions, food security and food safety in Lebanon was retrieved from the website of the ministry of public health.

The study investigated the level of abidance of 10 medium sized food industries (FI) in Mount Lebanon area in regard to allergen labeling through a phone call interview. The interview consisted of a questionnaire of 14 questions.

Results: Food allergen labeling regulations in Lebanon are governed basically by specifications of The Lebanese Standards Institution (LIBNOR) standard (NL206). It is also indirectly ruled by Consumer Protection Act No. 659; it protects consumer's right to be clearly, adequately informed and warned of the risks when consuming a product. Priority allergens on the LIBNOR list are similar to the Codex Alimentarius; they are not based on the incidence or prevalence of FA in Lebanon.

At the level of FI, LIBNOR was regarded as the main reference for food allergen labeling regulation and all 10 FI were 100% abiding by these regulations.

Conclusion: Epidemiological studies should be performed in order to assess the prevalence of FA in Lebanon. Therefore, priority allergen lists will be more representative of the Lebanese allergic population. It is recommended to have a unified easily accessible regulatory reference for FA management by the Lebanese law.

It is important to investigate at larger scale the abidance of FI in regard to allergen labeling in different areas of Lebanon. This will ensure the application of the legislation in regard to food allergen labeling.

TP1610 | Anaphylaxis to mushrooms (agaricus bisporus): A case report

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Background: We report a case of a 33 years old male with controlled allergic asthma and allergic rhinitis with sensitization to *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* that suffered an anaphylactic episode after eating cooked mushrooms. The episode occurred at the age of 25, minutes after eating a mushroom pizza. He reported facial and labial angioedema, dyspnea, cough and dysphagia. He denied physical exercise, alcohol or drugs consumption around the time of the meal.

He stopped eating all mushrooms and eats pizza without problems. He reports labial angioedema in two other occasions after accidental contact with mushroom sauce that took place after the mushroom pizza episode.

Method: Measure of total IgE and specific IgE to airborne allergenic sources, molds and mushroom were carried out.

We also performed skin prick tests (SPT) to commercial extracts of airborne, molds, mushroom and food allergenic sources and prick-to-prick test (PPT) to raw and cooked mushroom.

A SDS-PAGE *immunoblotting* assay was performed to assess the molecular mass of the IgE mushroom binding bands.

Results: Total IgE was 240 kU_A/L and specific IgE was positive to mushroom (0.76 kU_A/L), *Dermatophagoides peteronyssinus* (30.90 kU_A/L) and *Lepidoglyphus destructor* (2.33 kU_A/L) (Thermofisher, ImmunoCAP).

SPT were positive to *Dermatophagoides pteronyssinus* (10 mm), *Dermatophagoides farinae* (8 mm) and *Lepidoglyphus destrutor* (7 mm) (Prick Test LETI).

PPT was positive to raw (9 mm) and cooked (11 mm) white *Agaricus bisporus* and raw (14 mm) and cooked (11 mm) brown *Agaricus bisporus*.

Immunoblotting assay with *Agaricus Bisporus* extract revealed two main IgE binding bands of approximately 10 kDa and 26 kDa.

Conclusion: Allergy reactions to mushrooms ingestion are usually associated with IgE-cross reactivity between proteins from airborne molds and eatable mushrooms. Our patient presenting with a systemic reaction has a probable primary sensitization to mushrooms.

We were able to detect two IgE binding proteins with 10 kDa and 26 kDa as possible mushroom allergens.

TP1611 | Mushroom allergy: A case series

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Background: Mushrooms are the fruiting body of macrofungi mainly belonging to the Basidiomycotina and Ascomycotina divisions. They are consumed by many cultures worldwide and their consumption is increasing over the years. Nutritionally mushrooms contain vitamins and minerals. Fruiting season and cultivating region varies according to mushroom species. There are approximately 14 000 described mushroom species. IgE-mediated allergy to mushroom is rare. We report 4 cases of IgE-mediated allergy to mushrooms.

Method: We included patients diagnosed in our Allergy Department in 2018: 20-68 years old, 3 female and 1 male. All patients experienced immediate symptoms following consumption of cooked mushrooms. One patient experienced additional symptoms on cutaneous contact and inhalation. Symptoms ranged from angioedema and urticaria, gastrointestinal upset, light-headedness, dyspnoea

and throat tightness to localised skin irritation. One patient required emergency treatment.

Prick to prick tests (PPT) were performed to the raw and cooked caps of 11 mushroom species, except cep and morel which were rehydrated from dried form. Skin prick tests (SPT) were also performed to common aeroallergens with commercial extracts.

Results: PPT results to the index species (mushroom species eliciting symptoms) were positive in all patients. Interestingly, PPTs results (wheal size) to the cooked form of the index mushroom was 2-7 mm greater than the raw form. One patient showed a negative PPT result to the raw form of their index mushroom species and 7 mm wheal to the cooked form. There was a high degree of cross-reactivity between species belonging to the Agaricus genus. However, all patients cross-reacted outside the family of their index species indiscriminately. SPT results to fungal aeroallergens were positive in one patient. All patients had positive SPT results to tree, grass, weed or house dust mite.

Conclusion: We present, to our knowledge, the largest case series of mushroom allergy. We demonstrate the importance of identifying the culpable mushroom species and performing PPTs to both raw and cooked mushrooms when investigating mushroom allergy. Cooking is known to alter allergenicity of food proteins through denaturing, aggregation, glycosylation, promoting lipid biding and matrix effect. This case series also suggests, due to unpredictable cross-reactivity, patients allergic to mushrooms should avoid all mushrooms unless tolerance to specific species has been proved.

TP1612 | Anaphylaxis due to oat milk

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Background: Common oat or *Avena sativa*is a cereal belonging to *Poaceae* family. An increase in their consumption is taking place due to the fact that most celiac patients tolerates its ingestion. Oat allergy is not common but may occur. In fact, it is becoming more frequent due to the use of gluten-free diets among the celiac population.

Method: We describe the case of 62-year-old male with a personal history of ischemic heart disease, who developed an anaphylaxis after ingestion of oat milk. Within five minutes of taking oat milk, the patient presented oropharyngeal pruritus, dysphonia and dyspnea, followed by acute generalized urticaria, which required treatment in the emergency department with epinephrine, corticosteroids and antihistamines to resolve the symptomatology. The patient did not take NSAIDs or practice exercise previously and no other cofactors or possible triggers of the adverse reaction were associated. He did not report personal and familiar history of atopy, other episodes of anaphylaxis or previous adverse reactions. The patient cannot provide the assurance of having previously ingested oat milk. Currently he consumes cow's, soya and almond milks, as well as all cereals, except oat, without problems.

Results: Skin Prick test (SPT) performed with the most common aeroallergens in our region (dust mites, pollens, molds, pet dander) were all negative. Skin Prick test (SPT) performed with cereal extracts showed a positive result to oat (10 × 9 mm), maize (10 × 10 mm), wheat (7 × 6 mm), rice (5 × 5 mm) and barley (6 × 5 mm). Total IgE was 82.40 UI/mL. Serum specific IgE to cereal extracts were (ImmunoCAP system, Phadia, Uppsala, Sweden): 40.10 kU_A/Lto oat, 1.68 kU_A/L to wheat, 1.61 kU_A/L to maize, 2.70 kU_A/L to barley and 2.04 kU_A/L to rye. The protein profiles of oat seed and oat milk extracts were analyzed by SDS-PAGE, as described by Laemmli. SDS-PAGE immunoblotting was carried out in reducing conditions (with 2-mercaptoethanol) and pair of IgE binding bands of 55-kDa and a 45-kDa respectively, were revealed in both extracts; furthermore a 33-kDa band was detected in oat seed extract.

Conclusion: There are a very few studies on oat allergy and only two cases of anaphylaxis due to ingestion of oats have been published. We report a case of anaphylactic reaction following oat milk ingestion. The allergy workup revealed an IgE-mediated sensitization to oat and a non-symptomatic sensitization to other cereals.

TP1613 | Allergy to oat milk

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Background

Introduction: Oat (*Avena sativa*) is a cereal from the *Poaceaes* family widely used in our environment due to its high nutritional value; however, few cases of oat allergy have been described.

Method: Clinical case: We report a case of a 14-year-old male with a personal history of atopic dermatitis and bronchospasms to respiratory infections. He consulted because immediately after the ingestion of oat milk he presented pharyngeal pruritus in hands and foot and facial erythema. Previously he had presented oral pruritus with the ingestion of oat. He tolerates the ingestion of wheat and other cereals.

Results: Allergy study: Skin prick-test to oat extract was positive (6 × 6 mm); Total Ig E (IU/mL) 80; Specific IgE (CAP kU_A/L): oats 6.79; wheat 0.38; rye, barley, corn, rice, tri a19 and tri a14 < 0.35.

To study the molecular mass of the oat allergens involved, SDS-PAGE-Immunoblotting according to Laemmli was performed with oat milk and oat seed extracts using the patient's serum. IgE-binding bands of approximately 60 kDa, 50 kDa, 36/34 kDa, 25 kDa, 22 kDa were detected in oat seed extract, and bands of aprox. 59 kDa, 35 kDa, 29 kDa, 27 kDa and 22 kDa were revealed in oat milk extract.

Regarding the identity of the IgE-binding proteins detected, according to their molecular weights, the band of 34/36 kDa could correspond to the wheat allergen, Tri a 20, (molecular weight between 35-38 kDa) (which could justify a slight sensitization to the wheat allergen in our patient, the 23 kDa-band could be the 12S oat seed globulin, and the band around 50 kDa would correspond to a 48 kDa oat serpine previously described.

Conclusion: We described a case of IgE mediated reaction to oat milk with tolerance to other cereals.

Several protein bands with different molecular weights have been detected which could correspond to some oat and wheat allergens described above

TP1614 | Cow's milk allergy in adulthood

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Background: Cow's milk allergy (CMA) is the most frequent food allergy in children under three years old, but cases of CMA in adulthood are rare, with an estimated prevalence of 0.49-0.6%. CMA is likely to be more severe and persistent in adults. Previous studies show that spontaneous tolerance in CMA in adulthood rarely occurs and suggest that, during follow-up, a double-blinded placebo controlled oral challenge test should be used to assess tolerability.

Method: Clinical case.

Results: A 59-year-old female patient was referred to the Immunoallergology Consultation for anaphylaxis after ingesting cream and caramel ice cream. She suddenly began oropharyngeal itching, labial edema, difficulty swallowing and macular exanthema.

She attended to the emergency service and was treated with clemastine. The symptoms resolved in less than four hours. She did not eat ice cream again. Until the consultation she ate butter and drank coffee dripped with milk, but with associated oropharyngeal itch. Skin prick tests with commercial allergens (milk and protein, wheat, egg, shrimp, fish mixture, meat mixture, peanut, hazelnut) were positive for milk and casein. Total IgE (1098 KU / L) and specific IgE (kUA / L) was measured: milk 8.41, alpha-lactalbumin 0.01, beta-lactoglobulin 0.02, casein 13.30. The patient refuses to perform the oral provocation test. She avoids cow milk proteins, sheep and goat milk. She carries adrenaline in self-injecting pen, and a therapeutic plan with corticoid and oral antihistamine for use in case of accidental ingestion, according to the symptoms.

Conclusion: We present a case of CMA diagnosed in adulthood.

We pointed the persistence of allergy and the possibility of serious reactions, since the patient is sensitized to casein, and this protein is more often associated with exuberant reactions. The fact that the patient refuses to perform the provocation test difficult the evaluation of the acquisition of tolerance.

TP1615 | Allergy to chicken meat and chicken meat-dependent exercise-induced anaphylaxis: Case series

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Background: IgE-mediated hypersensitivity reactions to chicken meat is uncommon compared to egg, milk, peanuts and fish. There are reported cases in both adults and children but no reliable data on prevalence. Molecular analysis studies have identified α-parvalbumin to be the main allergen in chicken meat allergy.

Method: We describe three cases of atopic male patients with chicken meat allergy presenting in childhood.

Results: The first is a 36 year-old with multiple episodes of generalised urticaria and angioedema noted on exertion, within minutes following ingestion of poultry (chicken, duck, goose, turkey) and alcohol. He was diagnosed with food (poultry)-dependent co-factor induced allergy with positive skin prick test and specific IgE to chicken. The second is an 18 year-old who presented aged 8 with multiple episodes of sudden onset laryngeal irritation, coughing bouts and a sensation of a lump in his throat, occurring within a few mouthfuls of chicken meals. He was diagnosed with chicken allergy with positive skin prick test to chicken, and later outgrew the allergy at age 14. The third case is a 22 year-old with multiple episodes of anaphylaxis with lip and throat swelling, breathing difficulties and generalised pruritus occurring within ten minutes of ingesting chicken meals. Skin prick test to chicken was diagnostic and on avoiding chicken his symptoms resolved. The patients were prescribed oral anti-histamines and adrenaline auto-injector as emergency medication.

Conclusion: Although there are reported cases of chicken allergy, our first case is the first, to our knowledge, where chicken is associated with food-dependent co-factor (exercise and alcohol)-induced allergy. This highlights the repertoire of plant and animal proteins implicated in allergic reactions when co-factors such as exercise and alcohol are at play, is increasing. There is evidence for cross-reactivity between different poultry species (chicken, duck, turkey and goose), due to the structural homology of their α-parvalbumin. We therefore recommend that chicken allergic patients are advised of this potential risk and equipped with emergency treatment in case of accidental exposure. Interestingly, the α-parvalbumin in crocodile meat is also homologous to chicken α-parvalbumin with one reported case of cross-reactivity.

TP1616 | Cat-pork syndrome: A rare condition

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Background: Cat-pork syndrome is a rare condition, with few cases reported in literature. In this uncommon syndrome, patients develop

an IgE-mediate reaction to serum albumins present in cat that cross-reacts with porcine albumins.

Method: Retrospective analysis of medical records from a patient with a cat-pork syndrome.

Results: We report a case of a female with an history of intermittent moderate-severe allergic rhinitis and intermittent asthma when exposed to cat since childhood, treated with nasal steroids and antihistamines, referred to our allergy department with a recent history of generalized pruritus, wheezing and dyspnea few minutes after the ingestion of pork meat. She previously tolerated this meat and subsequently other meats particularly chicken, turkey, beef and rabbit. Skin prick tests (SPT) with meats and common aeroallergens extracts (Bial Arestegui®) were performed and positive to cat (10 mm), dog (5 mm) and pork (5.5 mm). Skin prick-to-prick tests (SPPT) were positive to cooked pork (8 mm) and negative to cooked chicken, turkey and beef. Specific IgE (ImmunoCAP Phadia®) were positive to cat (243 kUA/L), dog (43.4 kUA/L) and pork (21.30 kUA/L) and negative to chicken, turkey and beef. ISAC (ImmunoCAP Phadia®) was positive to specific components of some species, particularly, chicken (nGal d 5), cow (nBos d lactoferrin), cat (rFel d 1, rFel d 4) and dog (rCan f 5) and to some serum albumins involved in cross-reactivity, particularly, nFel d 2, nCan f 3, nEqu c 3, and nBos d 6. SDS PAGE IgE/immunoblotting assay is ongoing. A strict pork free diet was initiated and no more similar episodes occurred. She accidentally ingested smoked pork and few minutes later, a severe reaction occurred characterized by urticaria, angioedema and dyspnea. After this episode, no more accidental ingestions occurred.

Conclusion: Cat-Pork syndrome is rare, although it can lead to moderate to severe systemic reactions. This syndrome is related to cross-reactivity between serum albumins present in different animals. Cat Fed 2, dog Can f 3, horse Equ c 3 and cow Bos d 6 may explain cross-sensitization between furry animals and can be responsible for allergic reactions after meat consumption or airway exposure to animal hair or dander. In our patient, she only reported symptoms with exposure to cat and pork ingestion, despite sensitization to other furry animal and meat allergens.

TP1617 | Oral mite anaphylaxis; a case series from an Irish centre

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Background: Oral mite anaphylaxis (OMA) is a condition characterized by allergic symptoms after eating food prepared with wheat flour contaminated by storage mites.

Method: Medical records of patients with oral mite anaphylaxis diagnosed in a single centre over a three year period were reviewed. Patient demographics, presenting features and co-morbidities, along with diagnostic and management strategies were reviewed.

Results: 7 patients presented with OMA during this time frame (4 females, 3 males), mean age 28 years (15 – 55). Each patient experienced symptoms triggered by food made with wheat flour prepared by an occasional baker. 5/7 patients developed symptoms consistent with anaphylaxis requiring emergency department management. Diagnosis in each case was based on clinical history and supported by a positive IgE to storage mites *Acarus Siro*, *Lepidoglyphus destructor* and *Glycophagus domesticus*. A high degree of cross reactivity was identified. All patients were also strongly sensitised to house dust mite. All (7/7) patients had persistent allergic rhinitis, 4/7 had atopic asthma and 6/7 had a known background of intolerance to NSAIDs. In two cases, heavy mite contamination of the culprit wheat flour was confirmed using oil immersion microscopy. All patients were provided with an adrenaline autoinjector and given a written management plan including advice on asthma management and advice on storage of flour and other potential sources. No further reactions have occurred during follow up.

Conclusion: We describe a cohort of Irish patients with anaphylaxis to storage mite. A striking association with allergic rhinitis, asthma and NSAID intolerance was noted in this cohort. Confirmation of flour contamination by microscopy is very useful in affirming the relevance of mite sensitization test results. Clear avoidance advice is an essential part of management. A high index of suspicion is required to identify this fascinating and increasingly recognized condition.

TP1618 | Case of anaphylaxis due to pumpkin soup ingestion

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Case report

Background: Anaphylaxis, a form of IgE mediated hypersensitivity, is the most severe, potentially life-threatening allergic reaction. An anaphylactic reaction should be diagnosed and attended to as soon as possible with the best available treatment. Adequate follow-up and an etiological diagnosis are essential in addition to educating the patient and his family members or caregivers about possible new episodes. Food allergies are a common cause of anaphylaxis, estimated in 22.3% of the cases. Currently, the most useful test for the diagnosis of anaphylaxis is the measurement of serum tryptase, which should be requested when anaphylaxis is suspected. An enzyme curve should be performed in the first hour, at two hours and at 24 hours.

Case Presentation: We present a case of a 46-year-old male patient diagnosed with anaphylaxis by pumpkin seeds, who, after the ingestion of a pumpkin cream, starts 10 minutes later with epigastric pain, rhinitis, nasal obstruction, aphonia, facial erythema, throat discomfort with foreign body sensation, vomiting, slight dizziness, and without loss of consciousness. After assessing the results, he has a blood pressure of 114/77 mmHg, heart rate

73 beat/m, respiratory rate RR 18 rpm and a oxygen saturation (SaO2) of 97%, blood glucose of 95 mg/dl and temperature, 36°C. On physical examination, the patient presents with uvular angioedema, facial and thorax erythema. After treatment with adrenaline 0.3 mg im, 1000 cc serum therapy, dexchlorpheniramine 5 mg iv, hydrocortisone 200 mg iv and ranitidine 300 mg iv, he improves clinically and no longer has throat discomfort. After performing a complete analysis in the hospital, serum tryptase and seriation were not performed.

Conclusions: It is important to establish an agreed upon protocol, in the process of being patented, to carry out an etiological diagnosis and adequate follow-up, as well as educate the patient and his family members about possible new episodes of anaphylaxis.

TP1619 | Food-induced anaphylaxis as clinical form of pollen-food syndrome associated with recent onset seasonal allergic rhinitis due to ambrosia pollen sensitization. Case report

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Background: Pollen-food syndrome (PFS) is described as the association between pollen allergy and concomitant hypersensitivity reactions to a wide range of fruits, vegetables and spices, based on IgE cross-reactivity. This clinical entity, known before as oral allergy syndrome (OAS), may have rarely more severe forms, such as angioedema, urticaria, asthma or anaphylaxis.

Method: We report a case of anaphylactic reaction in a female patient aged 35 years, occurred 30 minutes after eating beef shawarma in a local restaurant, in October 2018. She has first addressed to Allergology Department of our university hospital one year before, for symptoms suggesting seasonal allergic rhino-conjunctivitis, with onset end July and lasting for about two months.

Results: In vitro testing showed very high level of serum specific IgE against two members of ragweed plant family - Ambrosia Artemisiifolia and Franseria Acanthicarpa pollen. She recognized having a lot of Ambrosia plants in the proximity of her living and working place. She did not follow our recommendation of sublingual specific immunotherapy and administered symptomatic therapy when symptoms reoccurred during the same period of the second year. She has no personal or family history of atopy and no previous food or drug allergy. No co-factors for anaphylaxis could be identified, such as exercise, alcohol, infections or medication. The food allergic reaction had sudden onset, with skin pruritus, lips and eyelids angioedema, dysphagia, dyspnea, epigastric pain, tinnitus and nasal obstruction, without hypotension. She was admitted to the closest hospital and treated with antihistamines and high doses systemic corticosteroids, without adrenaline and recovered in few hours. Serum tryptase and specific IgE against common foods performed after two weeks were normal. We have requested the composition of the meal and identified celery and coriander (cilantro), known to induce PFS associated with weed pollinosis, mainly the celery-mugwort-spice syndrome. Cross-reactivity between ragweed and mugwort is also well recognized. We recommended further allergologic evaluation and monitoring, due to severity potential of the condition.

Conclusion: The case is illustrative for the complex clinical significance of pollen allergies, reported to have an increasing prevalence worldwide.

TP1620 | Anaphylaxis to beluga caviar

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Case report: Introduction: Fish roe is an extremely rare cause of anaphylaxis and although its consumption has increased in recent years.

Methods: We described the case of a 59-year-old man, with no atopic history, who experienced an anaphylactic reaction after consuming one spoon of caviar beluga.

Skin prick-test were performed with Beluga caviar (from sturgeon), salmon caviar, cod, salmon, hen egg yolk and egg white. Specific IgE were also performed for hen egg yolk and egg white, ovalbumin, ovomucoid, parvalbumins (Gad c 1 et Cyp c 1), shrimp and mold.

Results: Only SPT to Beluga caviar was positive. The absence of sensitization to fish and hen egg was confirmed by undetectable specific IgEs to cod, parvalbumin (Gad c 1 and Cyp c 1),egg yolk and egg white, ovalbumin and ovomucoid. A immunoblot was also performed and showed an IgE-reactive band indicated that the patient was sensitized to a 26 kDa protein in Beluga caviar.

In our case, immunoblotting of the patient's serum revealed a single IgE-reactive band at 26 kDa band, which does not appear to correspond to the previous cases. Moreover, we can speculate that this protein is not a fragment of vitellogenin since another reactive band would likely have been found in this instance.

Conclusion: Our patient presented a selective food allergy to Beluga caviar. The resulting sensitization appeared to be due to a 25 kDa protein, which has not been described previously.

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PRIMARY IMMUNODEFICIENCIES

TP1621 | C4 deficiency and familial inheritance

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Background: Complement component C4 is a protein part of the complement system. C4 deficiency is associated with a number of autoimmune diseases and recurrent pyogenic infections.

Method: We have evaluated 2 female patients : mother (37 years) and daughter (7 years). Both of them suffered many episodes of mild and moderate (mother) and mild (daughter) urinary infections from early childhood (age of three). Many of them required courses of antibiotherapy. The mother also presented in the last year long periods of cutaneous lesions with aspect of chronic urticaria. Patients were investigated in two steps: first at the initial presentation and second in a moment of apparent health. Both of them were evaluated for: complete blood count, CRP, ESR, rheumatoid factor, fibrinogen, C3 and C4 complement, immunogram (IgA, IgE, IgG, IgM), electrophoresis, urinalysis, urine culture, thyroid antibodies (Thyroid Peroxidase Antibody (TPO) and Thyroglobulin Antibody (TGAb)).

Results: After the first evaluation we have obtained the following abnormal results : mother – urinalysis : leucocytes 30/µl, urine culture : *E. coli*, TPO 39.1 IU/mL (N.V < 5.61 IU/mL), TGAb 24.82 IU/mL (N.V < 4.61 IU/mL), C4 7.9 mg/dl (N.V 15-57 mg/dl); daughter – urinalysis : leucocytes 25/µl, urine culture : *E. coli*, C4 4.9 mg/dl. After a course of antibiotherapy and in an apparent state of health we have repeated the analysis and obtained the following results : mother C4 11.2 mg/dl and daughter C4 8.9 mg/dl. The mother was diagnosed of having Hashimoto thyroiditis and both of them with mild C4 deficiency. This results explain the medical history of the patients and are congruent with medical literature.

Conclusion: C4 deficiency is an important health problem due to predisposition to infection. We have shown the importance of evaluating offsprings of a patient with C4 deficiency because of its possible family inheritance. This case is one of the first that describe a possible inheritance of C4 deficiency through generations Future larger genetics and family studies will reveal the exact genetic mechanism of transmission.

TP1623 | Late-onset combined immunodeficiency: A case report

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Case report: Common variable immunodeficiency (CVID) represents the most frequent symptomatic primary antibody disorder, characterized by hypogammaglobulinemia. Several immune and genetic factors cooperate to define the complex spectrum of disease manifestations, that includes not only an increased risk of infections, but also others disease related complications (such as autoimmunity, enteropathy, lymphoproliferative disorders).

We described the case of a 47 year-old-man that come to our attention for 10 year history of hypogammaglobulinemia with recurrent infections of the upper and lower airways, recently complicated by a severe sepsis from an opportunistic agent (Candida spp, herpes simplex) and an ischemic stroke, from which he has recovered. In his past history, diabetes mellitus type 2, dyslipidemia with atherosclerotic carotid stenosis and systemic arterial hypertension. He referred profound asthenia and diarrhea with negative cultures. At the clinical examination, any specific sign was found. Lab analysis showed a severe IgA, IgM and IgG deficiency with a low CD4 count and low switched memory B cells. The diagnosis of late onset combined immunodeficiency (LOCID) was established and treatment with intravenous immunoglobulin (IVIg) 20 g every 3 weeks was started.

LOCID represents a subgroup of CVID patients with associated severe T cells deficiency (with CD4 < 10% or < 200/nL) and/or opportunistic infections. LOCI patients may differ in several features compared with CVID ones with an increased prevalence of splenomegaly, granuloma, gastrointestinal disease, and lymphoma, and even on immunoglobulin substitution, they may require more frequent antibiotics administration and hospitalization.

TP1624 | A strange case of CVID-associated granulomatous disease

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Case report: Common Variable Immunodeficiency Disorders (CVID) consist of a heterogeneous group of conditions with different clinical patterns. Less than 20% of cases have a defined monogenic cause, so CVID is often considered a polygenic and multifactorial disease. Granulomatous disease (GD) occurs in 8%-22% of patients and can be rarely associated to non-cirrhotic portal hypertension (NCPH). We describe the case of a woman suffering

from CVID complicated by GD-NCPH, with single nucleotide variations in three CVID-associated genes. A 56-year-old woman affected by CVID came to our attention for recurrent digestive hemorrhages. Anamnesis includes primary hypoparathyroidism, interstitial lung disease, familiarity for CVID and autoimmune disorders. On physical examination, the patient appeared pale, with abdominal distension and hepatosplenomegaly. Blood test showed pancytopenia and anicteric cholestasis, without signs of hepatic failure, and excluded the most frequent causes of hepatopathy. Abdominal CT and gastroscopy respectively showed moderate ascites and oesophageal varices. Transient elastography was suggestive of cirrhosis. The hepatic biopsy revealed a granulomatous hepatitis with initial signs of portal fibrosis, excluding the diagnosis of cirrhosis and defining the rare condition of NCPH connected to GD. Considering the family history and the rarity of the clinical setting, we decided to screen the patient for CVID-associated genetic mutations.

The patient was treated with prednisone 1 mg/kg/die, facilitated subcutaneous immunoglobulin, diuretic therapy and propranolol. After six months, ascites and pancytopenia reduced and no more episodes of digestive hemorrhages occurred, without significant infections connected to the immunosuppressive therapy. The genetical analysis showed single nucleotide variants in three loci: WAS (known for Wiskott-Aldrich Syndrome), DOCK2 (involved in CVID and Cold Urticaria) and PLCG2 (CVID). These mutations, which are reported in international databases, still remain of uncertain clinical meaning.

NCPH GD-associated is a rare condition that can occur in patient affected by CVID. We found in our patient three single nucleotide variants in genes already known for causing antibody deficiency. Even if these variants remain of unknown significance, it is reasonable to suppose that they can be implied in a polygenic genesis of CVID, contributing in this case to the development of GD.

TP1625 | Clinical presentation of granulomatous lymphocytic intersticial lung disease (GLILD) in a referral center in brazil

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Case report: This study describes 4 clinical presentations of patients diagnosed with GLILD in the Clinical Immunology Division of the Hospital das Clínicas of the Federal University of Minas Gerais.

Patient 1 - Female, 19 years, diagnosis of CVID 2 years ago. In August 2016 due to splenomegaly, neutropenia and thrombocytopenia underwent splenectomy. Spleen biopsy showed nonspecific lymphocyte proliferation. Then, was diagnosed with chronic pulmonary inflammatory process due to nodular proliferations at the pulmonary parenchyma. The patient refused treatment with corticosteroids and awaited immunohistochemistry (IHC) for therapeutic definition.

Patient 2 - Female, 35 years, diagnosis of CIVD for 12 years with loss of follow-up. In 2017, she returned to the service with splenomegaly and weight loss. In January 2018, CT evidenced pulmonary nodules, thoracic lymph node enlargement and portal hypertension, and a biopsy demonstrated nodules with lymphoid hyperplasia. IHC demonstrated abundant CD-3 T lymphocytes in the paracortical region and CD-20 B lymphocytes in the cortical zone. Prednisone 20 mg/day was initiated, with a 4 cm reduction in spleen size in the first month of treatment.

Patient 3 - Male, 50 years, diagnosis of CVID 2 years ago. In June 2017 CT scan revealed mediastinal lymphadenopathy and hypersplenism. Lymph node biopsy showed reactive lymphoid hyperplasia with Castleman pattern areas and extensive granulomatous reaction. IHC with findings indicative of possible histiocytic proliferation (positive for CD3, CD20 and CD5 + /+++). Castleman's disease was excluded after haematological investigation. Pulmonary biopsy revealed epithelial microgranules and lymphohistiocytic inflammation, and therapy with prednisone was initiated.

Patient 4- Female, 13 years, diagnosis of CVID, liver fibrosis, sclerosing cholangitis and hemolytic anemia. Splenectomy was performed in March 2017 due to splenomegaly and splenic necrosis. In June of 2018 it evolved with respiratory insufficiency and pulmonary hypertension. Pulmonary biopsy demonstrated interstitial lymphoplasmacytic inflammatory infiltrate associated with rare granulomas. After initiation of prednisone, there was a significant improvement in the respiratory pattern and hospital discharge.

This description of the cases is important to demonstrate different presentations of this little known disease. The remaining patients are undergoing outpatient follow-up and show significant improvement after corticotherapy.

TP1626 | Is the incidence of gastric tumor increasing in variable common immunodeficiency patients?

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Background: Common variable immunodeficiency (CVID) is a group of heterogeneous diseases characterized by increased susceptibility to sinopulmonary and gastrointestinal infections, cancer, inflammatory diseases and autoimmunity. Several studies have demonstrated high prevalence of lymphoma followed by gastric cancer in these patients. Objective: to evaluate the prevalence of gastric tumors in a cohort of 179 outpatients with CVID from 1982 to 2018, accompanied at the Division of Clinical Immunology and Allergy at HCFMUSP, São Paulo, Brazil.

Method: Retrospective review of medical records of 179 adults patients with CVID.

Results: We evaluated 179 patients: 97 women (54.18%) and we observed that 35 patients (19.55%) presented cancer; thirteen of them (37.14%) had gastric tumor (Tu); seven patients (53.84%) were women, 8 (61.53%) caucasians, 4 (30.76%) afro-descendants and 1 (7.70%) indigenous. The mean age at onset of clinical manifestations of CVID was 13.23 ± 10.47 years and the mean age at diagnosis (Dx) was 33.62 ± 14.11 years. The mean delay in between the onset of clinical manifestations of CVID and diagnosis was 20.38 ± 11.43 years and the mean time of human immunoglobulin reposition (IVIg) was 21.42 ± 13.90 years. The average disease time of all CVID patients was 36 ± 9.61 years, the mean age at Tu diagnosis was 45.15 ± 11.03 years, mean of ICV time when Tu Dx was 30.80 ± 8.69, mean of the Tu evolution time 26.08 ± 22.35 months. Twelve patients (92.30%) had Adenocarcinoma and one patient had a well differentiated neuroendocrine Tumor grade I. Five patients (38.46%) evolved to death with time of evolution of Tu 48.60 ± 73.99 months. No statistical differences were found when we assessed the means of the ages above in the group that survived and in the death group. Ten patients (76.92%) had gastric atrophy, autoimmune diseases and lymphocytic alterations, 11 (84.62%) had intestinal metaplasia, 7 (53.85%) had H pylori (+) and all had chronic diarrhea and IgA deficiency. We observed an increase in the prevalence of gastric tumors in the last years, with the incidence of 1982-2013: 0.23 new cases/year and 2014 to 2019: 1.20 new cases/year

Conclusion: Our data differ from the literature because most of our patients presented Tu gastric, even though they underwent endoscopy every year. We also observed an increase in incidence of Tu gastric in the last five years without known cause. We did not find statistical differences between the group that survived and those that died.

TP1627 | LRBA deficiency in three patients, single center experience

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Case report

Background: The mutations in LRBA gene causes LRBA deficiency that is characterized by recurrent infections, hypogammaglobulinemia, lymphoproliferation and autoimmunity. Here, we present 3 cases with LRBA deficiency.

Patient 1 is a 36-year-old female admitted to our clinic with the complaint of recurrent lung infections, persistent diarrhea, and splenomegaly. She had Hashimoto thyroiditis at the age of 15 years. There was a consanguineous marriage between her parents. The immunologic evaluation showed lymphopenia, markedly low IgG, IgA and IgM levels and low CD4 lymphocytes. A novel homozygous insertion in *LRBA* (c.7238dupG, p.S2413Rfs*1) was provided kindly by G. Uzel. IVIG replacement therapy was started at the diagnosis. The chest CT showed mediastinal multiple lymph nodes, cystic bronchiectasis, diffuse frosted glass densities and some consolidations.. Her pulmonary findings receded following CTLA4-Ig (abatacept) treatment.

Patient 2 was a 14-year-old boy, younger brother of Patient 1, applied to our clinics with recurrent infections and hepatosplenomegaly. Bone marrow biopsy showed hemophagocytosis. The immunological investigations showed low IgG, A, and M levels; a reversed CD4/CD8 ratio, positive anticardiolipin IgM and direct Coombs antibodies. His thorax CT showed the ground glass view, *mediastinal* nodes, and bronchiectasis in both lungs. He had been treated with IVIG every three weeks. At the age of 11, chemotherapy was started according to HLH 2004 protocol. He died at the age of 14 due to pulmonary infection. Twelve years later, LRBA mutation was detected in his sister. Therefore, genetic analysis was performed on his spleen and the same mutation was confirmed.

Patient 3 is a 17-year-old female, who admitted to our clinic with recurrent otitis, sinusitis and sinopulmonary infection. There were intractable diarrhea, nausea and inadequate weight gain in her medical history. She had hearing loss due to recurrent otitis. Autoimmune pancytopenia developed at the 15 years old. Meanwhile, regular IVIG therapy was started due to hypogammaglobulinemia, pneumonia, and concomitant cytopenia. Septal thickening in both lungs and several nodules was detected in her thorax CT. Following IVIg and CTLA4-Ig treatment, her complaints have decreased.

Conclusion: LRBA deficiency should be considered in cases having immunodeficiency and autoimmune manifestations Abatacept is a promising treatment for LRBA deficiency.

TP1628 | Two cases with homozygous TACI mutation; could TACI mutation be a cause of microcephaly and growth retardation?

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Case report

Background: Transmembrane activator and CAML interactor (TACI) controls T cell-independent B cell antibody responses, isotype switching, B cell homeostasis and mediates immunoglobulins production. Homozygous mutations in TACI have been reported rarely. Here, a homozygous TACI gene defect was detected in two patients who have antibody production defect. *A 33 year old female* admitted to our clinic with recurrent pneumonia, recurrent ear infections, malnutrition, intermittent swelling of bilateral parotid glands since 28 years old. There was a second-degree consanguinity between her parents. Her older brother died because of lymphoma. Physical examination revealed massive splenomegaly, hepatomegaly, lymphadenomegaly, crepitations in the lungs and abdominal distension. Leukopenia, thrombocytopenia, low serum IgG, M and A levels and direct coombs positivity were found in her laboratory. Widespread nodules in the lungs associated with

ground-glass density and atelectasis were detected in her chest CT. Parotid gland needle biopsy showed chronic sialadenitis, benign epithelial cells and lymphocytes. The bone marrow biopsy was normal. She diagnosed as CVID (common variable immunodeficiency) and immunoglobulin replacement therapy was started. She was homozygous for a reported deleterious change in *TNFRSF13B* encoding TACI (c.310T>C, p.C104R). Although taking IVIG therapy regularly, she died due to pneumonia at 42 years old. *A fourteen year old male* admitted to our clinics with recurrent respiratory infections since his infancy period. There was a third-degree consanguinity between his parents. Physical examination revealed growth retardation (<3 percentile), microcephaly (<3 percentiles), splenomegaly and hepatomegaly. Anemia, leukopenia, thrombocytopenia, low serum IgG, M and A levels were found. Many lymph nodes were detected in the mediastinum and retroperitoneal area by his chest and abdominal CT. His liver tissue biopsy showed mild lymphocytic inflammation and the bone barrow biopsy was normal. A homozygous mutation (c.204dupA/p.Leu69Thrfs*12) in TNFRSF13B (NM_012452.2) gene was detected. He is doing well with immunoglobulin replacement therapy.

Conclusion: TACI mutations are a rare cause of CVID. To our knowledge our second patient is the first case having a homozygous c.204dupA/p.Leu 69Th fs*12 mutation in TNFRSF13B gene in the literature. Besides, hypogammaglobulinemia and recurrent infections, he had microcephaly and short stature.

TP1629 | Primary hemophagocytic syndrome: Description of new mutation in a patient at a referral center in brazil

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Case report: The objective of this case report is to demonstrate a clinical case of hemophagocytic syndrome, with associated genetic diagnosis.

A seven months of age girl, previously healthy, was admitted at the Hospital das Clínicas da UFMG in December 2016 for investigation of anemia, thrombocytopenia and neutropenia associated with hepatosplenomegaly, diagnosed after clinical irritability and pallor. She carried out extensive infectious and hematological propaedeutic without definitive diagnosis. The diagnosis of myelodysplasia was initially considered by myelogram findings. She needed several transfusions and numerous treatments for febrile neutropenia. In April 2017, she started with strabismus and left eye ptosis. Magnetic resonance imaging demonstrated thickening and exuberant contrast enhancement of the left oculomotor nerve, with neurite characteristics. In one episode of febrile neutropenia in May 2017, the patient presented with bilirubin increase at the expense of direct bilirubin, in addition to an increase in transaminases, canalicular enzymes, triglycerides and ferritin, leading to the diagnosis of hemophagocytic syndrome. She performed genetic sequencing, which demonstrated mutation in heterozygosis in two genes associated with HLH: a variant of uncertain significance in the STX11(c.429G>T: p.M143I) and a probably benign in STXBP2 (c.1654A>G:p.R552G). Allogeneic hematopoietic cell transplantation was performed with unrelated donor 10/10, source in bone marrow. However, patient presented graft failure. In addition to cyclosporin, immunosuppression with methylprednisolone was initiated for serum sickness, with normalization of hematocrit indices. Any attempt to reduce it has been associated with changes in the blood count, mainly thrombocytopenia. At the moment the patient remains well, at 2 years and 8 months, waiting for programming of a new transplantation of hematopoietic stem cells.

Discussion: It was a case of difficult diagnosis due to a not typical clinical findings initially, that was confirmed with genetic test with new mutation, in heterozygosis in the gene STX11, gene with high frequency of mutations relative to the primary hemophagocytic syndrome.

TP1630 | Refractory chronic urticaria treated with omalizumab in a young adult with common variable immunodeficiency

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Case report: M.K. is a 19-year-old female adult, who suffered of recurrent lower respiratory tract infections requiring hospitalization since early childhood. At 10 years of age, M.K. also started experiencing chronic diffuse urticaria (i.e., itching wheals for > 6 weeks), not apparently elicited by any specific factor and sometimes associated with cough and dyspnea. At 15 years of age, due to recurrent respiratory and cutaneous symptoms, she undertook immunological exams, which showed significant reduction in the levels of IgG (-3 SD) and IgM (-1 SD), a reduction of CD19 lymphocytes (58/mm3) and absence of antibody response against common vaccinating antigens, supporting the diagnosis of common variable immunodeficiency (CVID). Analysis for known genetic causes of hypogammaglobinemia came out negative. A replacement treatment with subcutaneous human immunoglobulin (5 g/weekly) was started. Despite an improvement in infective episodes following immunoglobulin replacement therapy, M.K. continued to experience refractory chronic urticaria. At that time the Urticaria Activity Score over 7 days (UAS7) was 42/42 points, despite being treated with combination of 2nd-generation H1-antihistamines at high dose and oral steroid. The diagnostic work-up recommended by the EAACI/GA²LEN/EDF/WAO guideline (i.e., Zuberbier T et al, Allergy 2018) for chronic urticaria was then performed, resulting inconclusive. Therefore, considering the strong impairment on everyday quality of life, an add-on treatment with omalizumab (300 mg/month) was started, resulting in complete remission of urticaria after the very first injection, with no

further need of antihistamines and steroid. So far, MK has received 8 injections of omalizumab, reporting no side-effects. The anti-IgE monoclonal antibody omalizumab is recommended as a third-line treatment of severe refractory chronic urticaria. However, safety and efficacy of such biological therapy is not known when chronic urticaria coexists with CVID, because patients affected with primary immunodeficiency are usually excluded from clinical trials on biologics. This is the first case of refractory chronic urticaria successfully treated with omalizumab in a young adult affected with CVID. Despite the limitations deriving from a single case analysis, this report evidences that omalizumab is also a safe therapeutic option for patients with chronic urticarial and concomitant CVID.

TP1632 | Amyloidosis in patients with common variable immunodeficiency: A rare event associated with severe outcome

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Background: Common variable immunodeficiency (CVID) is the most common form of severe antibody deficiency. Secondary amyloidosis is a rare and serious complication of CVID, and is usually seen in men in the middle age group. In this paper, we report two cases of CVID with amyloidosis.

Method: Case 1: A 32-year-old male patient was admitted with the complaints of cough, diarrhea and weight loss. He has been receiving monthly IVIG treatment for 12 years. In the physical examination of the patient, his general condition was poor and coarse rales were heard in the left lung and pretibial and scrotal edema was observed. Laboratory tests revealed reduced total protein and albumin and proteinuria. Immunological evaluation revealed hypogammaglobulinemia. Bronchiectasis, pleural effusion, intraabdominal acid, and pericardial effusion were observed in radiological examinations. Amyloidosis was found in histopathological examination of biopsy of abdominal fat tissue. Case 2: A 45-year-old male patient presented with sputum cough, dyspnea, watery diarrhea and weight loss. The patient has had frequent respiratory tract infections since childhood. He had bronchiectasis five years ago and was treated with IVIG for 1 year with the diagnosis of CVID. In the physical examination rales were heard in both lungs. Bronchiectasis was present in radiological examinations. hypogammaglobulinemia and proteinuria were detected in the patient. He underwent colonoscopy and a biopsy taken from various sites, including the rectum. CMV colitis and amyloidosis were detected. The IVIG treatments that were taken by both patients were rearranged weekly due to ongoing proteinuria.

Results: However, after a while both of the patients died from massive proteinuria, renal failure, chronic lung disease and cardiogenic shock.

Conclusion: When proteinuria was detected in CVID patients, amyloidosis must always come to mind and IVIG therapy should be individualized taking into consideration the patient's metabolic status.

TP1633 | Chronic granulomatous disease in a patient with rhodococcus equi in palmas-TO-brazil. Case report

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Case report: Chronic granulomatous disease (CGD) is a primary immunodeficiency characterized by recurrent infections. Is rare with an incidence of 1:250 000 live births. In immune system phagocytes contain a membrane associated NADPH oxidase that produces superoxide and other reactive oxygen intermediates, which is responsible for microbicidal, tumoricidal and inflammatory activity. In CGD this system shows alteration of human phagocytic NADPH oxidase, which leads to serious and potentially lethal infections. We report a 5-month-old-boy with CGD who presented invasive pulmonary infection by *Rhodococcus equi* in Palmas-TO, Brazil, diagnosis confirmed by biopsy, epidemiology and positive therapeutic test. Histological analysis of lung tissue reveals a mixed process with occasional giant cells. The interior of the alveoli demonstrates lipophages. The special PAS and FIT FARACO stains show inside these tiny structures, gram-positive cocco-bacillary bacterium. Morphological findings, associated with epidemiological and social antecedents, exclude Legionellosis, Mycoplasma, Tuberculosis, Atypical mycobacteriosis, Aspiration of alimentary content, but strongly raises the possibility of Rhodococcosis. Other tests with negative results. *Rhodococcus equi* is the species of greatest pathogenic potential for animals including humans. Hydrogen Peroxide Test/ Dihydrorhodamine confirmed CGD. Is a soil organism carried through the intestine of herbivores and diffused into its environment. Its pathogenic potential results from the ability to persist in the destruction of macrophages. So this patient presented high morbidity with serious clinical repercussions.

TP1634 | The expediency of combined immune-rehabilitation in the treatment of primary immunodeficiency in humoral type

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Background: Isolated replacement therapy of primary a (hypo) gammaglobulinemia does not lead to the complete leveling of immunodeficiency clinical manifestation, but the use of antibiotics may be limited to side effects. Search of alternative methods of reactivation of chronic inflammatory diseases prevention is actual. The purpose of the research is to study the effectiveness of combined immunotherapy in patients with primary a (hypo) gammaglobulinemia.

Method: 10 patients aged 18-60 years (men-6, women-4) with the diagnosis of CVID (6 people) and XLA (4 people) were under observation. All patients received IVIG therapy (0.4 g/kg of body weight, monthly) and additional correction with muramyl peptide immunomodulator at a dose of 200 mg № 5 intramuscularly every other day, every three months three courses. Flow cytofluorimetry method was used to study peripheral blood and assess the parameters of innate and adaptive immunity.

Results: All patients had relapses of chronic sinusitis, chronic bronchitis, an average of 6 ± 1 episodes per year with a duration of 15 ± 3 days before the administration of combined therapy. Within six months of combined therapy three people were not registered with exacerbations of chronic inflammation foci, the incidence averaged 0.9 ± 0.5 with a duration of 10 ± 4 days. Comparing the parameters of the immune system a month after the first course of the immunomodulator with the initial data showed an increase in the number of circulating CD8 + -T effectors (48.2 ± 5.18%; in the outcome of 40.5 ± 2.58%). Three months later, there was an increase in the expression of activation markers on T-effectors (CD8 + HLA DR + 18.9 ± 4.04%, in the outcome of 5.38 ± 1.18%) and pattern-recognizing receptors on monocytes (CD14 + TLR4 + 40.8 ± 4.1%, in the outcome of 26.9 ± 7.7%). In six months of follow-up, after two courses of combined therapy, not only the effect on the number and expression of t-cell activation markers was observed, but also the occurrence of an additional criterion for their high cytotoxic activity:CD8 + Gr + 33.8 ± 2.9%; in the outcome 24.6 ± 3.49%).

Conclusion: The use of combined therapy in patients with primary a-(Hypo)agammaglobulinemia has contributed to reducing the frequency of exacerbations of chronic inflammatory diseases. The positive clinical effect is associated with the activation of the functional properties of T-lymphocytes and monocytes. Stabilization of effects is possible at multiplicity of use of muramyl peptide immunomodulator once in three months.

TP1635 | Cerebral ischemic attacks in ADA2 deficiency treated with adalimumab

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Case Report:

Background: Adenosine deaminase deficiency type 2 (ADA2) is an autosomal recessive disorder caused by loss of function (LOF) mutation in ADA2. It is characterized by early onset vasculopathy, livedo racemosa, mild immunodeficiency, systemic and CNS manifestations. The first described monogenic vasculitis is ADA2 deficiency. Here, we described a girl with ADA2 deficiency who suffered from severe neutropenia and transient cerebral ischemic attacks.

Case: A seventeen years old female patient presented with recurrent fever, lymphadenopathy, gingivitis, loss of teeth, and recurrent skin infections when she was two years old. Physical examination revealed multiple lymphadenomegalies on the submandibular and submental area and hepatosplenomegaly. Laboratory examination revealed neutropenia (532/μL). The excisional biopsy taken from the submandibular lymph node showed non-specific *reactive changes* in the *lymph node*. Bone marrow biopsy was normal except for decreased myeloid series. HAX1, ELA2 defects were excluded by Germeshausen's laboratory. G-CSF was started as 5 micrograms/kg/day because of recurrent aphthous stomatitis and skin abscess. At the age of 15, she had recurrent syncope attacks. The evaluation of cardiovascular and neurologic systems were normal. The cranial MRI was normal. A frameshift mutation (p.Arg49Alafs) was detected in the CECR1 gene by Raif Geha's lab. Adalimumab treatment was started 40 mg (SC) every 2 weeks. Her syncope attacks lost following adalimumab treatment, but neutropenia has sustained.

Conclusion: ADA2 deficiency is a rare and multifaced vasculitis syndrome. Neutropenia is an extremely rare manifestation of this illness. Although our patient did not have a livedoid skin rash, she had transient ischemic attacks of the brain suggesting cerebral vasculitis. As a conclusion, ADA2 deficiency should be considered in cases with neutropenia, lymphoid hyperplasia, and cerebral vasculitis. Adalimumab is an effective agent to prevent cerebral ischemic attacks.

TP1637 | Autoimmune and inflammatory diseases in primary immune deficiencies

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Background: Autoimmune and inflammatory diseases can be seen in primary immunodeficiencies related to defective immune response and immune dysregulation.

TABLE 1. The distribution of primary immunodeficiencies in our patient cohort

	n	%
CVID	5	35.7
XLA	2	14.3
LRBA	2	14.3
TACI	2	14.3
CTLA4	1	7.1
MSH6 deficiency	1	7.1
Good syndrome	1	7.1

TABLE 2. Autoimmune and inflammatory diseases and autoantibodies of the patients.

Autoimmune and inflammatory diseases	n	%
Hashimoto thyroiditis	4	28.6
Lung Granuloma	4	28.6
Recurrent parotitis	2	14.3
Lymphoproliferative disorder	3	21.4
Systemic lupus erythematosus	1	7.1
Crohn Disease	1	7.1
Oligoarticular JIA	1	7.1
Behçet's Disease	1	7.1
Psoriasis	2	14.3
Autoimmune hemolytic anemia	1	7.1
Immune thrombocytopenic purpura	1	7.1
Autoantibodies		
Anti-Thyroid Peroxidase	3	21.4
Anti-Nuclear Antibody	2	14.3
Direct Coombs	2	14.3
p ANCA	1	7.1
Anti-Histone antibody	1	7.1
Anti-ds DNA	1	7.1
Anti Ro 52	1	7.1
Anti-thrombocyte antibody	1	7.1
Anti-basal membrane antibody	1	7.1

Method: Fourteen patients with primary immunodeficiencies and autoinflammatory manifestations were included in the study. The data were obtained from the electronic files of the patients retrospectively. **Results**: The female/ male ratio was 6/8, the median age of patients was 28 years (minimum = 11, maximum = 58 years) and the median age of diagnosis of immunodeficiency was 22 years (minimum = 4, maximum = 52 years). The rate of autoimmune and/or inflammatory diseases was 19.4%. CVID was the most common PID caused autoinflammatory conditions in our cohort (n = 5, 35.7%), others were shown in table 1. Hashimoto thyroiditis and granuloma in the lungs are the most common autoinflammatory diseases (n = 4, 28.5%). Autoimmune and /or inflammatory diseases; and autoantibodies of the patients were shown in table 2. The most common accompanying disease was chronic lung disease (n = 9, 64.2%).

Conclusion: Autoimmune and inflammatory diseases are common in primary immunodeficiencies. Primary immunodeficiencies should also be questioned in patients who had autoimmune and inflammatory diseases associated with recurrent infections.

TP1638 | Two rare cases in one patient

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Case Report:

Background: An Armenian boy in age 4 y.o. was diagnosed with X-linked agammaglobulinemia (XLA) after pneumonia. Genetic testing has approved the diagnosis with a followed mutation - c. 185 G>C, pR61P. After diagnose he has given intravenous immunoglobulin G 10 mg per month. Also, flow cytometry was done and the result for B cell marker is CD19 - 0. Several years the boy's medical history was unremarkable after diagnose. He has started complaining of abdominal pain, recurrent pain in joints, periodic fever. Another genetic testing was done after excluding several infections. It revealed two mutations in Mediterranean fever gene - V726A, E148Q. The diagnosis of familial Mediterranean fever was made. After genetic confirmation colchicine was prescribed. Now, two rare diseases are under control. The boy is 3rd patient in the same family.

Familial Mediterranean fever is an autoinflammatory disease caused by mutations in the MEFV gene, which encodes a 781–amino acid protein called pyrin. The mutated pyrin causes high inflammatory activity leading to increased IL-1β production and NF-kB activation. In fact, FMF is a common disease in Armenia. The MEFV mutations carrier state in Armenia is 1:3. The most frequent mutations are M694V, M680I, V726A, E148Q. Colchicine is the drug of choice for FMF since 1972 for preventing the acute attacks and development of secondary amyloidosis – the most devastating complication of FMF. Colchicine prevents FMF attacks in more than 60% of FMF patients and significantly reduces the number of attacks in another 20%-30%. 5%-10% of FMF patients do not respond to therapy. The biologics are recommended too (IL-1 receptor antagonist, anti-TNF antibody). The combination of these two rare diseases is extremely rare, but we need suspect in case of Armenian origin of a patient.

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MOLECULAR PROFILE AND ALLERGY EPIDEMIOLOGY

TP1639 | Pattern of sensitization to common aeroallergens in the north of Portugal: Four-year evaluation of an allergy center of a university hospital

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Background: Aeroallergens play a major role in the pathogenesis of the allergic disease. The sensitization profiles vary according to genetic predisposition, geographical areas of residence and patient's age. We aimed to characterize the sensitization pattern to aeroallergens of patients sent for allergy testing in the last four years and compare sensitization profiles between adults and children.

Method: This was a retrospective observational study based on the results of all aeroallergens skin prick tests (SPT) performed at an university hospital centre in the north of Portugal between 2014 and 2018 (n = 10463). SPT were performed according to the European standards (*Heinzerling et al of 2013*). Tests belonging to the same patient (n = 559) were reviewed to match a single case; the information was supplemented and the most recent tests were considered. False negatives [negative histamine] (n = 151) and false positives [positive saline solution] (n = 60) were excluded.

The adult panel included the following allergens: *D.pteronyssinus*(Dp), *D.farinae*(Df), *L.Destructor*(LD), dog dander, cat dander, plane, birch, olive, grass mix, weeds mix, Parietaria, *Cladosporium herbarum* (Ch), *Aspergillus fumigatus*(Af) and cockroach. The children panel (<5 years) included Dp, Ld, grass mix, weeds mix and cat dander extracts.

Results: A total of 9694 patients, 60% female with a median age of 25 [13; 43] years (34% children) were evaluated corresponding to 10252 tests.

Regarding the test results, 48% were positive for Dp, 37% for Df, 39% for Ld, 19% for dog, 17% for cat, 8% for plane, 6% for birch, 14% for olive, 34% for grass, 18% for weeds pollen, 9% for Parietaria, 4% for Ch, 3% for Af and 6% for cockroach; 85% of patients were polysensitized.

Sensitization to Dp, Df and grass pollen were more prevalent among children ($P < 0.001$), but sensitization to dog, plane, birch, olive, Parietaria, Ch, Af, cockroach and weeds pollen were significantly more frequent in adults. Adults were more frequently polysensitized than children ($P = 0.036$). In monosensitized children the most involved allergen was Dp (49%) whereas in adults was Ld (31%).

Conclusion: In our sample there was a high prevalence of sensitization to house dust mite and grass pollen. Age dependent differences in aeroallergens follows the trends observed in populations from other countries, where the occurrence of sensitization to inhalant allergens increases with the age.

TP1640 | Current sensitization profile of allergic patients in Southern Slovakia - analysis of 6726 patients from one outpatient clinic

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Background: Slovakia is a Central European country. The southwestern part of Slovakia belongs to the Cfb area (heat, damp, hot) according to Köppen-Geiger's geoclimatic classification, while the rest of the country belongs to the Dfb zone (snow, damp, hot summer). We were interested in the current sensitization profile of patients from Nitra region (southwest) and, in particular, prevalence of sensitization to so-called invasive plant species, including *Ambrosia* (regweed).

Method: This is a retrospective analysis of skin prick test in 6726 patients who have visited our Outpatient Clinical Immunology and Allergology Department from January 2013 until December 2018. We analyzed the test results for mites, birch, ash, grass, mugwort, ragweed, cat, dog and *Alternaria*.

Results: At least one positive test was found in 2895 (43.04%) patients from whole examined group (n = 6726). Most common were pollen (2371, 81.97%), followed by mites (1038, 35.85%), pets (874, 30.19%) and Alternaria (851, 29.40%). In pollen allergy, there is predominantly sensitization to grass (1608; 73.98% of pollen allergy), followed by mugwort (*Artemisia*) (1186; 52.22%), birch (*Betulla*) (1126; 49.58%) and finally by ragweed (*Ambrosia*) (1049; 46.19%).

Conclusion: Our analysis has confirmed that the most common allergy in this part of Slovakia is grass pollen allergy. At the second place is allergy to pollens of mugwort followed by birch. Although ragweed is the last one, we were surprised by its high prevalence. Up to 46.19% of patients sensitized to pollen, respectively 36.23% of all allergic patients were sensitized to *Ambrosia*. This represents almost 15.6% of surveyed population.

TP1641 | Ragweed pollinosis epidemy in Bratislava, Slovakia

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Background: Despite ragweed is not natural in Europe, in last decades the contamination of environment with its pollen is alarming and the number of suffering patients is increasing. In our outpatient

department we monitor the changes in sensitisation profile of patients during years.

Method: Patients with pollinosis are routinely tested by prick tests and specific IgE. In the past only extract based diagnostics were used, in last years we use also molecular (component resolved) diagnostics. We compared the sensitisation profile of our patients evaluated in years 1999-2002 and in the year 2018. More than 600 randomly selected patients were included. As clinically relevant we rate allergen which is positive in prick test and patient has symptoms during pollen season of positively tested plant.

Results: In the year 1999 we rated by prick test as clinically relevant grasses in 72%, birch in 38% and mugwort or ragweed (*Asteraceae* family) in 31%. In patients sensitised by *Asteraceae* we evaluated mugwort more clinically relevant than ragweed. The results were similar when evaluating percentage of positive specific IgE (sIgE) antibodies. But interestingly we find out that the amount of ragweed sIgE (kU/L) was significantly higher than that of mugwort antibodies. The percentage of polysensitised patients increased significantly during years. In 1999-2002 it was 55%, in 2018 it increased to 82.5%. In 2018 there was no significant difference in sensitisation by grass (80%), birch (78%), ragweed (78%) and mugwort /(72%) pollen according to prick test. The result was similar when using sIgE diagnostics with pollen extracts. But the result was completely different when using molecular diagnostics. Main birch allergen Bet v1 was positive in 90% of patients with average value o sIgE 16.65 kU/L, main grass allergen Phl p1 was positive in 83% patients with sIgE = 8.15 kU/L, main ragweed allergen Amb a1 was positive in 73% patients with sIgE = 18.96 kU/L, main mugwort allergen Art v1 was positive only in 41% with sIgE = only 2.63 kIU/L.

Conclusion: We see shift to polysensitisation in population of patients with pollinosis in Bratislava. Also we see the increasing clinical importance of ragweed pollen in our region. According to molecular diagnosis of sIgE we see higher clinical significance of ragweed pollen in comparison with mugwort and grass pollen, either we suppose higher aggressiveness of ragweed pollen. Following our results we emphasise the urgent need for allergen immunotherapy preparation with ragweed pollen.

TP1643 | Prevalence of sensitization to indoor allergens and its major components in Lithuania

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Background: The aim of our study was to determine the frequency of sensitization to the indoor allergens and their components in patients with allergic rhinitis/rhinoconjunctivitis or/and allergic asthma and to compare the results with neighbour countries.

Method: Blood samples were taken from 106 patients with allergic rhinitis/rhinoconjunctivitis or/and allergic asthma from the August 2017 till the April 2018. Specific (s) IgE against cat, dog and house dust mites (HDM) extracts and main components were measured.

Results: This study included 106 participants (69 women and 37 men, age 18-87 years). Patients were sensitized mainly to *D. farinae* and *D.pteronyssinus* (55.6% and 50.0% accordingly). Less than half of tested samples had sIgE to cat and dog extracts (43.0% and 34.9%). No significant difference between gender and age groups were found. Out of patients whom were sensitized to cat allergen extract 89.1% had sensitization to Fel d 1, 17.4% to Fel d 2 and 39.1% to Fel d 4. From those who were sensitized to dog allergen extract, 62.2% had sensitization to Can f 1, 27.0% to Can f 2, 10.8% to Can f 3, and 37.8% to Can f 5. Those, sensitized to HDM were positive to Der p 1 (56.6%), Der p 2 (64.2%), Der p 10 (3.8%) and Der p 23 (54.7%). If monosensitization was detected Fel d 1 was the most frequent allergen and reactivity to it was detected in 56.5% monosensitized individuals.

Discussion: Comparing sensitization rates to cats our results are in concordance with findings in Poland, Russia and Spain. In Sweden, different population was tested (atopic dermatitis (AD) patients) and only 52% were sensitized to Fel d 1 and 24% to Fel d 4.

Our results related to patients sensitization to dogs differs from Poland's (40.0% to Can f 1 and 31.4% to Can f 5). Only 24% patients with AD were sensitized to Can f 1 and 22% to Can f 5 in Sweden. In Central European study sensitization to HDM components was lower: 19.0% to Der p 1 and 25.1% to Der p 2. Similar results to this study were found in Sweden.

Conclusion: The sensitization range to major indoor allergens differs in different countries. Larger studies of patients with various allergic diseases as well as in healthy population are needed.

TP1644 | Patterns of molecular sensitization in adults in Dnipro region (Ukraine)

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Background: Patterns of sensitization may vary in different regions even within the same country. The data about molecular sensitization profile in eastern Ukraine is still lacking.

Method: Medical history, anthropometry, clinical examination, total serum IgE and specific IgE to allergen extracts and allergen molecules (multiplex assay ALEX®) were evaluated in all patients.

Results: 77 patients 18-61 years old (39 men) with any history of allergic diseases were included in the study. 84.4 % of them had asthma; 84.4 % – allergic rhinitis; 63.6 % –signs of skin allergy. Total serum IgE was 112.00 [32.00-273.00] kU\L. 35 patients (45.5 %) had total serum IgE less than 100 kU\L.

In accordance with serum specific IgE to allergen extracts the most common sensitization was to ragweed (64.9 %); sagebrush (55.8 %) and birch (49.4 %). More than 30 % of patients were sensitized to

timothy, oat and chaff. More than 20% had sensitization to hazelnut pollen, olive, alder, cherry tree, sunflower seeds. Sensitization to house dust mite was detected in 27.3 % patients. The most common pet's allergen was cat (19.5 %). In accordance with test results for the IgE to allergen molecules the most frequent sensitization was detected for Amb a 1 (68.8 %); Art v 1 (44.2 %); Bet v 2 (40.3 %); Pho d 2 (40.3%); Aln g 1 (37.7 %); Bet v 1 (36.4 %); Mal d 3 (36.4 %). More than 30 % patients were sensitive to Lol p 1; Amb a 4; Phl p 1; Der f 2; Alt a 1. More than 20% – to Ole e 2; Ole e 1; Fel d 1; Act d 1; Der f 1; Der p 1; Der p 2; Cup a 1. The sensitizations for other tested molecules were less than 10%. It should be noted that high sensitization level for some molecules were detected in patients with normal total IgE.

Conclusion: 1.Adult patients with history of allergic diseases in Dnipro region (Ukraine) more often sensitized to the grass and trees pollen. The most common specific serum IgE were for Amb a 1 (68.83%); Art v 1 (44.15%); Bet v 2 (40.25%); Pho d 2 (40.25%); Aln g 1 (37.66%); Bet v 1 (36.36%).

2.The most common food allergen was Mal d 3; pet allergen – Fel d 1; house dust mite – Der f 2.

3.The pattern of sensitization evaluated by serum IgE to extracts and molecular allergens are not entirely similar. Thus, identifying specific IgE to allergen molecules is useful tool for improve the diagnostic accuracy and detect the cross reactivity.

TP1645 | Features of molecular diagnostics in patients with asthma and allergic rhinitis

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Background: To study the effect of diagnostics on the appointment of allergen-specific immunotherapy in patients with asthma and allergic rhinitis (AR).

Method: The study involved 50 patients within 22 to 49 years, 62% of women and 38% of men with AR and asthma in Kharkiv region hospital. The study included standard research methods, computer spirometry (SpiroCom, KhAI Medica, Ukraine), asthma control test ACQ-5, endoscopic examination of the nasal mucosa, molecular diagnosis of allergen extracts by ELISA (ALEX, Austria).

Results: In all patients, insufficient control of asthma was revealed, FEV1 -on average - 69.3%, ACQ-5 - on average 2.1 points, in 34 patients - seasonal AR (SAR). The patients with burdened AR inheritance, oral allergy syndrome in 5 patients, complaints of sneezing, itching in the eyes and nose, discharge of watery secretions from the nose, difficulty breathing, insufficient asthma control, swelling of the nasal mucous membranes, molecular diagnosis - on average - 15.2 kUa/L, Bet V1 -11 patients, Amb a 1 + Art V 1 in 12 patients, Amb a 1 in 5 patients, Art V1 in 4 patients, Art V3 in 2 patients. Identified apple sensitization in the SAR group Mal d 2 - on average 3.6 kUa/L in 8 patients. Chronic AR (CAR) identified in 16 patients, symptoms were present nasal breathing difficulty, dry nasal mucosa, hyposmia, hyperplasia of the lower shells of the nasal mucosa, hight titers allergens in molecular diagnosis on average 4.5 kUa/L Der P1 - 6 patients, Der P2 - 3 patients, Der F2 - 4 patients, Hev b1 - 3 patients and 5 patients had cats, was confirmed by a high level FEl d 1 on average 3.6 kUa/L.

Conclusion: Conducting molecular diagnostics, along with standard research methods of AR and asthma, makes it possible to understand the structure of sensitization, improve asthma control, reduce the symptoms of AR, decrease the need for provocative tests and allow reasonably to conduct allergen-specific immunotherapy.

TP1648 | Modern view on management of allergic diseases in Kazakhstan

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Background: The development of diagnostics of allergic diseases started in Kazakhstan since the 1960s, the discovery of the immunoglobulin (IgE) antibody provided a specific biomarker that could be used to identify allergic diseases triggered by environmental allergens. Traditional IgE antibody tests such as skin prick tests (SPT) or in vitro specific IgE (sIgE) tests are based on crude extracts composed of allergenic and non-allergenic molecules obtained from an allergenic source. The availability of allergenic molecules in the last decade has ushered in a new phase of diagnostics, termed molecular-based allergy diagnostics, that allows for improved management of allergic diseases.

Method: Currently three steps for testing of allergic diseases in Kazakhstan are: I – skin testing; II – Ig E detection; III – molecular allergology, an approach used to map the allergen sensitization of a patient at the molecular level, using purified natural or recombinant allergens instead of allergen extracts.

Results: Molecular allergology gives increased accuracy in allergy diagnosis and prognosis including: 1) resolving genuine versus cross-reactive sensitization in poly-sensitized patients, thereby improving the understanding of triggering allergens; 2) assessing, in selected cases, the risk of severe, systemic versus mild, local reactions in food allergy, thereby reducing unnecessary anxiety for the patient and the need for food challenge testing; 3) identifying patients and triggering allergens for the most accurate specific immunotherapy (SIT). In Kazakhstan serum Ig E initially by radioallergosorbent test in 1980-1990, revealed high values of serum Ig E corresponding to 1000 KU/L or higher in 90% patients, and then by means of Immunochemical assay in 1990-2010 (UNICAP) determination of allergen-specific Ig E antibodies revealed in the majority of patients prevalence of reaction to weeds - sage, ragweed, then meadow plants (cocksfoot grass, timothy, foxtail), and seldom to trees (birch,

poplar). There was revealed acute sensitization associated with domestic and epidermal allergens reaching high values. Lower values of Ig E associated with food-borne allergens.

Conclusion: Polysensitization in the population of the Republic of Kazakhstan is very common.

TP1649 | Allergic sensitisation in asthmatic patients followed up at a central hospital in Landa, Angola

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Background: Allergic sensitisation depends on the relationship between genetic susceptibility and exposure to allergens. Climatic conditions, socioeconomic and local cultural aspects may predispose to sensitisation by different allergens according to the studied region. Knowledge about these regional profiles is important to defining environmental control measures and prescription of allergen-specific immunotherapy. There are very few studies of allergic sensitisation in adults, in Africa and, in Angola, no such studies have been performed. Thus, the aim of this study was to analyse the profile of allergic sensitisation in asthmatic patients.

Method: This was a cross sectional study, conducted from April to November 2018, with patients aged 18 years old or over, with clinically confirmed diagnosis of bronchial asthma, followed up at Pulmonology outpatient clinics, at the Military Hospital in Luanda. Allergic sensitisation was defined by skin prick tests (SPT) with a battery of aeroallergens, in the presence of weals with a mean diameter of at least 3 mm any of the inhalant allergens tested, with negative reaction in the negative control and papule at the site of histamine of at least 3 mm. Asthmatic patients with a history of pulmonary tuberculosis and patients with Chronic Obstructive Pulmonary Disease (COPD) were excluded. Data were analysed with SPSS Statistics v25.0.

Results: The sample consisted of 230 patients [mean age - 41.9, median - 41.0 (18 to 86 years)], 56.5% female. Of these 72.6% had isolated asthma and 24.8% had asthma and allergic rhinitis. Of the 230 patients, 65.7% (151 patients) had positive SPT with most frequent sensitisation being to mites (*B. tropicalis*, *Der. farinae*, *Der. pteronyssinus*), cat and dog epithelia, fungi (*A. alternata*, *C. herbarum*, *M. mucedo*, *A. fumigatus)* and cockroach mix, without statistically significant differences between sexes. Of the patients with positive SPT, 76.2% were polysensitised and 23.8% were monosensitised.

Conclusion: Allergic sensitisation to dust mites, dog and cat epithelium, fungi and cockroach mix is the most frequent pattern observed in adult asthmatic Angolans living in Luanda.

TP1650 | Analysis of distribution characteristics of TIgE and SIgE in patients with respiratory allergic diseases

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Background: To explore the distribution characteristics of serum total immunoglobulin E (tIgE) and specific immunoglobulin E (sIgE) in patients with respiratory allergic disease.

Method: A total of 1129 patients with respiratory allergic disease were detected serum tIgE and sIgE by fluorescence enzyme-linked immunosorbent assay. The average age was 12 (7, 42.5) years old. SPSS 22.0 software was used for statistical analysis.

Results: The positive rate of tIgE of the patients enrolled in the study was 81.85%. As the age group grow up, the peak of tIgE positive rate appeared in 7~16 years old group, the positive rate was 94.33%. Then the positive rate decreased to 61.47% in ≥ 60 years old group. The average level of tIgE of male was higher than female[293.0(110.0, 730.3) kU/L vs 184.0(69.0, 468.0) kU/L]. The difference was statistically significant (Z = -5.288, $P < 0.001$). The major inhaled allergens of patients with respiratory allergic disease were Dermatophagoides farinae 84.43% (347/411), house dust mites 66.96% (756/1129) and tropical mites 63.10% (106/168) and the major food allergens were shrimp 27.12%(147/542), milk 26.23% (107/408) and egg white 22.11%(88/398). The sensitization peak of house dust mites, Dermatophagoides farinae, tropical mites, cat dander and dog dander appeared in 7~16 years old group, Aspergillus fumigatus appeared in ≥ 60 years old group. The correlation between house dust mites and Dermatophagoides farinae was the highest in inhaled allergens (r_s=0.937, $P < 0.001$), shrimp and crap was the highest in food allergens(r_s=0.928, $P < 0.001$), Blatella germanica and shrimp was the highest in inhaled and food allergens(r_s=0.881, $P < 0.001$).

Conclusion: Adolescent stage is the sensitization peak of inhaled allergens in patients with respiratory allergic disease. In addition to the common inhaled allergens, the detection of mould fungi sIgE cannot be ignored for the elderly patients.

TP1651 | A pilot study on the allergen-specific IgE to molecular components on polysensitized mite allergic asthmatic patients in Guangzhou, China

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Background: Using multiplex microarray-based component resolved diagnosis (CRD) to investigate the allergen sensitization profile of allergic asthma patients in southern China.

Method: Serum samples from 57 polysensitized mite allergic asthmatic patients in a tertiary referral centre of southern China were tested with multiplex CRD (ISAC) for specific immunoglobulin E (sIgE) against 112 single allergen and components. Result was then compared with those from singleplex ImmunoCAP.

Results: With ISAC, the highest sensitization was seen for nDer f 1 (71.9%), rDer f 2 (73.7%), nDer p 1 (70.2%) and rDer p 2 (66.7%), whereas rDer p 10 and other storage mites' components only showed 10% positivity. rFel d 1 and rCan f 1 were found positive in 29.8% and 14.0% samples respectively. Other epithelia components had less than 7.0% positive rate. Sensitization to pollen components was dominated by nCyn d 1 (17.5%) and nPhl p 4 (12.3%), Carbohydrate cross-reactive determinants (CCD) was positive in 4 patients who were also positive to nPhl p 4, nCyn d 1 and rPla a 2, and all of them have combined asthma and rhinitis. The sensitivity to mold (rAsp f 3), cockroach (nBla g 7) and *Anisakis simplex* component (rAni s 3) were all the same at 8.8%. 93.0% patients were sensitive to more than one component, with more than half of them (57.9%) positive to five or more components. Patients with combined asthma and rhinitis (AA+AR) were sensitive to more components than those with asthma only (AA). Positive rate to nPhl p 4 was significantly higher in patients with AA+AR than with AA only ($\chi^2 = 4.31$, $P = 0.038$).

Compared with ImmunoCAP, ISAC showed a similar high detection rate for *D. pteronyssinus* and *D. farinae*, but only 10.0% of *B. tropicalis* sensitive patients were positive to rBlo t 5. Optimal scale analysis on correlation of allergens components showed rDer p 10 was associated to food allergy.

Conclusion: Being the first multiplex microarray based CRD study on southern Chinese, ISAC showed house dust mites components were the major allergen components led to sensitization in asthmatic patients. Patients with combined AA+AR were sensitive to more components than those with AA only. Other components with higher positive rate include pollen components nCyn d 1, nPhl P 4 and animal dander components rFel d 1 and rCan f 1. For *B. tropicalis*, the rBlo t 5 in ISAC may not represent the major *Blomia* component in southern Chinese patients.

TP1652 | Trends in skin prick test according seasons: Results of a Korean multi-center study

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Background: Allergy is a very common condition. Allergic disease is highly affected by environmental changes. Conditions of the four seasons change dramatically in Republic of Korea (ROK). The aim of this study was to assess changes in the rates of aeroallergen positivity according to seasons and environmental factors: temperature, humidity, and precipitation.

Method: In total, 20 hospitals were selected based on the population distribution in ROK. A skin prick test (SPT) panel, comprising 55 aeroallergens, was distributed to 18 hospitals for a prospective study. Results from SPTs done in 2006 and 2010 were collected and analyzed retrospectively from 20 hospitals, and the 2014/2015 SPT (from June 2014 to May 2015) results prospectively from 18 hospitals.

Results: We compared the allergen-positive rates among seasons. Positive test rates for several pollens and house dust mites increased significantly in spring and fall. Pollens positive rate varied significantly according to temperature, precipitation, and humidity, while mite allergens were less susceptible to environment.

Conclusion: There are four distinct seasons in ROK. The positivity of pollen allergens were especially affected by the temperature and precipitation in spring. In other hands, House dust mites were affected by seasons, temperature, precipitation and humidity less than the pollen. Therefore, regular follow-up and re-evaluation of allergic test are essential considering the change of seasons and environment for acceptable diagnosis and treatment.

TP1653 | Evaluation of a population with and without rhinitis in a tropical city

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Background: Nasal obstruction is a common symptom of rhinitis and is often secondary to decreased nasal patency. Anatomy and physiologic causes of nasal obstruction include septal deviations, inferior turbinate hypertrophy, sinonasal inflammatory conditions and nasal cycle. The primary endpoint of this study is to describe nasal cavity findings in patients with and without rhinitis through anterior rhinoscopy, and compared them with the clinical findings through acoustic rhinometry in a second phase.

Method: Anterior rhinoscopy was performed in 127 subjects, older than 5 years, with chronic rhinitis (n = 93) and healthy control subjects (n = 34) to compare the findings obtained with this technique. There were no significant differences between the study groups (rhinitis vs control) and the demographic characteristics like age and gender.

Results: 5.9% healthy control subjects and 16.1% rhinitis subjects had surgical history, adenoidectomy being the most common. Rhinorrhoea and nasal septal defect findings, were not statistically different between the study groups. 52.9% healthy control subjects had turbinate changes, with the non-contact right nasal cycle (50%) as the most common. 77.4% rhinitis patients had turbinate changes, the most frequent of which being non-contact left nasal cycle (30.5%), non-contact right nasal cycle (26.4%), and contact left nasal cycle (19.4%). There were statistically significant differences between the study groups and the findings in the turbinate changes ($P = 0.028$).

Conclusion: Anterior rhinoscopy is a subjective and simple method to evaluate the nasal cavity. Acoustic rhinometry is an objective technique used to assess nasal obstruction as its measures nasal

cavity area and volume. We present our study initial results which compares the nasal cavity findings in patients with and without rhinitis through anterior rhinoscopy.

TP1654 | IgE- sensitization patterns from three different populations

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Background: In this study the specific IgE pattern of sensitized persons from 3 different populations from 3 different geographical areas has been investigated. The European samples were from the Tyrol, Austria, representing a northern temperate climate. The first Asian group is from southern China, representing a humid subtropical climate and the second Asian group, Central-Asian samples from Uzbekistan, representing a dry continental climate.

Method: 101 Austrian, 14 Chinese and 127 Uzbek samples were included in this study. All samples were tested with ALEX®-Allergy Explorer – an IgE-multiplex test, which enables the simultaneous detection of 282 different allergen extracts or molecular allergen components.

Results: According to this study, it could be demonstrated that 50%-60% of the sensitized persons in the Austrian population have specific IgE antibodies against grass pollens, e.g. timothy, and rye grass. Around 50% show IgE antibodies against cat allergen Fel d 1, followed by a sensitization rate of 45%-50% against mites. The dominant mite species are of the Dermatophagoides family. The most prevalent components were Der p/f 1 Der p/f 2 and Der p 23. Next most common are sensitizations against tree pollens, 40%, where the dominant component sensitization is related to PR-10 proteins. The major food allergens are cherry, kiwi and peanut with a prevalence around 15%. The Chinese samples show very different IgE-pattern were a high prevalence for different seafood such as crab, lobster and oyster related to tropomyosin were seen. The occurrence of mite-specific antibodies is comparable to the Austrian population (40%-50%); however, mites as Blomia are represented in this population. Other detected foods are Litchi, oat and papaya and nuts that showed a higher prevalence rate compared to the Austrian and Uzbek samples. Almost no IgE against trees and weeds was found. The Uzbek samples display some similar patterns when it comes to grasses and cats. However, some weeds such as salsola and mugwort show a high prevalence of 20%-30%. Mite sensitization is rare, less than 3% in this population. Of the foods peach and papaya show a sensitization rate of 10%-15%. The dry climate may have an impact to the low prevalence of mite-specific IgE antibodies.

Conclusion: The different sensitization patterns presumably reflect the different environments of the studied populations. With this information health systems can respond accordingly in prevention and therapy.

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ALLERGEN EXTRACTS AND MOLECULES FOR VETERINARY ALLERGOLOGY

TP1655 | Variability in Fel D1 in cats is unrelated to cat phenotype but decreases with age

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Background: Fel d1 is the primary allergen affecting cat-allergic individuals. Fel d1 is produced in several glands including the salivary glands, then distributed to the haircoat during grooming. The goal of this study was to evaluate variability of salivary Fel d1 by time or phenotypic characteristics of age, gender, weight, hair coat color and pattern.
Method: Neutered female and male adult cats were enrolled into a study conducted at two locations, in Missouri, USA (Group 1; n = 27) and in Ontario, Canada (Group 2; n = 37). All cats were followed for one year: Group 1 beginning in spring and Group 2 beginning in autumn. Saliva was collected twice a day, every other day, using salivettes (Sarstedt, Germany). Samples were stored at −80°C until analysis using a Fel d1 ELISA kit (Indoor Technologies, USA). Data were evaluated using a linear mixed-model analysis to determine effects of time and cat characteristics. on salivary Fel d1.
Results: Salivary Fel d1 averaged 6.3 ± 7.8 μg/mL for Group 1 and 8.1 ± 12.8 μg/mL for Group 2, with overall range from non-detectable to 322.1 μg/mL. The skewed distribution represented intra-cat and inter-cat variation. Cats with low average Fel d1 tended to have low variability while cats with higher average Fel d1 showed greater intra-cat variability. Salivary Fel d1 was unrelated to sex, body weight or hair coat characteristics, but did differ by age, with lower Fel d1 noted among older cats ($P < 0.001$).
Conclusion: This study provides data on the variability of salivary Fel d1 both within and among cats and will be important for future studies.

TP1656 | Allergy approach to a dog population from a veterinary dermatology consultation at the tropical inland city of londrina, Paraná, Brazil

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Background: Prevalence of allergy in dogs is also increasing associated with better living conditions and medical care. Indoor life is more often related to mite and mold sensitization and allergy, while an outdoor environment would favor a pollinic response with seasonal worsening. On the other hand, food allergy tends to present as a perennial condition. The particular frame of a tropical climate may in turn introduce environmental factors associated either with the concentration of available airborne allergens or skin barrier conditions. This study *aimed* to characterize the allergy frame of a dog population attending the State University of Londrina and Veterinary Clinics Life Space dermatology outpatient consultation, situated in the tropical inland region of Paraná, Brazil
Method: A 111 allergic patient population (60 males and 51 females) was selected by clinical evaluation and submitted to food allergy restriction measures from 2015 to 2018. Thirty five patients (33.3%) belonged to predisposed breeds, 74.8% were indoor and 25.2% outdoor.
Results: First signs started between 1-3 years of age in 55% of the patients and after the 3 years in 45%. Several comorbidities were found in 47.5% of the 1-3 years group and in 60% of the above group. Atopic dermatitis (AD) was diagnosed in 90.9% and food allergy (FA) in 23.7%, with 12.6% of simultaneous AD+FA. *Malassezia* overgrowth (MO) was diagnosed in 49.6% of the patients, mostly in the AD group. Flea allergy dermatitis was simultaneously diagnosed in 14.4% of the patients and otitis and conjunctivitis in 36% and 18.9%, respectively. Skin barrier disruption with seborrhea was diagnosed in 59% of the patients. The fourth version of the Canine Atopic Dermatitis Extent and Severity Index (CADESI-4) showed 13.5%, 33.3% and 53.2% of Light, Moderate and Severe scores, respectively, and pretty similar in the group of predisposed-breeds. Positive correlation was found between CADESI-4 scores and FA ($P = 0.03$), seborrhea ($P < 0.00001$), MO ($P = 0.00003$) and otitis ($P = 0.01$). *Malassezia* overgrowth correlated positively with indoor living ($P = 0.02$) and otitis ($P < 0.00001$) despite 29% of MO without otitis. Simultaneous flea allergy correlated negatively with MO ($P = 0.0079$), otitis ($P = 0.001$) and conjunctivitis ($P < 0.00001$).
Conclusion: A clear clinical worsening trend was found associated with seborrhea, FA, indoor living and otitis and MO in this tropical population. *Malassezia* overgrowth is probably more severe in this wet tropical environment.

TP1657 | Development of a new dermatophagoides farinae extract for its specific use in allergic dogs

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Background: Canine atopic dermatitis is a pruritic allergic skin disease, being *Dermatophagoides farinae* one of the main non-seasonal responsible agents. Different profiles of sensitization to *D. farinae* have been described between human and dogs. High molecular weight (MW) proteins, Der f 15 and Der f 18, are major allergens in dogs, while groups 1 and 2 are considered major allergens for humans. Despite these differences, allergic dogs have traditionally been treated using extracts intended for human immunotherapy. This study aims to develop a specific allergen extract for veterinary practice enriched in the major allergens for dogs and to demonstrate the *in vitro* efficacy of the extract.

Method: The veterinary allergen extract was manufactured from a *D. farinae* culture by protein extraction, ultrafiltration and lyophilization, looking for an allergenic composition adapted for allergic dogs. A *D. farinae* extract used for human immunotherapy was used as control. Relative quantification was estimated by densitometry for Der f 15 and Der f 18 and by mass-spectrometry analysis for Der f 15. The protein profile was analyzed by SDS-PAGE and size exclusion chromatography (SEC). Allergenic profile was studied by immunoblot and biological potency calculated by direct ELISA and ELISA inhibition assays using serum samples from atopic dogs (n = 16). Extracts immunogenicity was analyzed by determining the production of IL-10 and IFN-ϒ cytokines by peripheral blood mononuclear cells from atopic and healthy dogs (n = 6).

Results: The veterinary extract showed a higher content of high MW proteins respect to the control. These proteins were recognized with a higher intensity by the pool of sera. The fold-increase of Der f 15 and Der f 18 respect to human extract was 2.3 and 2.5, respectively, by densitometry analysis, and 2.97 (Der f 15) by mass-spectrometry analysis. The different MW distribution of both extracts was confirmed by SEC. All serum samples presented significantly higher specific IgE levels against veterinary extract and a biological potency more than 2 times higher (0.062 *vs*. 0.132 μg for 50% inhibition) was found for veterinary extract. The new extract induced significantly higher levels of IL-10 (1748 pg/mL) and IFN-ϒ (50.4 pg/mL) respect to the negative control.

Conclusion: A veterinary *D. farinae* extract with a higher content of dog major allergens Der f 15 and Der f 18 has been developed and its *in vitro* efficacy demonstrated by immunological parameters.

TP1658 | Dermatological and allergy approach to a dog population from a veterinary consultation at the tropical coastal city of São Paulo, Brazil

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Background: Dermatological problems are between the major reasons for dog veterinary consultation, with allergic pruritic conditions playing a relevant and increasing role. Besides genetic predisposition associated with sensitization and skin barrier imbalance, indoor/outdoor life is also associated with different level of exposure to several airborne allergens. Food allergy is also a known condition requiring clinical and food trials for specific diagnosis. Itch is a common sign associated to pruritic conditions like atopic or food allergy dermatitis, resulting in frequent skin infections. Diversity and concentration of airborne allergens as well as skin barrier condition may in turn vary according to environmental conditions, influencing the pattern of sensitization and allergy. Hence, this study *aimed* to identify the patterns of skin allergy in dogs of the city of São Paulo, Brazil, a highly populated tropical coastal area.

Method: An 84 mostly allergic dog patient population (45 males and 39 females) attending the Pompeia Veterinary Hospital outpatient consultation was selected from 2015 to 2017 by clinical evaluation and submitted to food allergy restriction measures. Thirty one patients (36.9%) belonged to predisposed breeds, 77.4% were indoor and 22.6% outdoor.

Results: First signs started from the age of 2 months to 11 years old. Several comorbidities were found in 23.5% of the 1-3 years old group and in 29% of the above group. Atopic dermatitis (AD) was diagnosed in 69% of the patients and food allergy (FA) in 4.8%, but no simultaneous AD+FA was found. *Malassezia* overgrowth (MO) was diagnosed in 58.3% of the patients, half of them, including 5 from predisposed breeds, lacking a diagnosis of allergy. Flea allergy dermatitis was diagnosed in only one patient with no AD nor FA, but presenting MO. Bacterial otitis was observed in 6% of the patients, either with AD or AD+MO. *Malassezia* overgrowth correlated positively with outdoor living ($P = 0.009$) but negatively with AD. Food allergy correlated positively with an increasing age at the onset of signs ($P = 0.01$).

Conclusion: Although roughly one-third of AD-patients presented with MO, this has been frequently observed as the only diagnosed cause of dermatitis, associated with outdoor living, which could be probably related to the local perennial warm and wet climate. The FA onset of signs associated with a higher age should follow further investigation regarding the implicated food.

TP1659 | Investigate the impact of cat allergen from different cat breeds on cat sensitized subject using novel progenitor cell derived basophil activation test

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Background: Cat ownership is often used as an indicator for cat allergen exposure. However, the variability between cat breeds and cat behaviour which may affect how much allergen cats carry on the hair, is difficult to take into account, including how this might impact cat owners who are sensitized to cat allergen. The aim of this pilot study is to compare how cat sensitized subjects responded to cat allergen prepared from different cat breeds, using progenitor cell derived basophil activation tests (PCBAT).

Method: Cat allergens were extracted from clipped hair of four domestic cats; three mixed breed, and one pure breed (Bengal, considered as "hypoallergenic"). All allergen preparations were standardized by preparing 1 gram of cat hair in 2 ml of extraction buffer. Progenitor cell derived basophils (PCB) were differentiated from $CD34^+$ progenitor cells. Serum from one cat-sensitized subject (skin prick test > 3 mm) and one cat non-sensitized subject (skin prick test negative) was used to passively sensitize the PCB cultures. The cultures were then stimulated by incubating with a range of different dilutions of each of the four extracted cat allergen extracts. Percentage cell degranulation was measured using β-hexosaminidase assay.

Results: The PCBAT to the four different cat allergens extracts showed different trajectories. For all four allergen extracts, the dose-response curves reached a plateau at higher concentrations of allergen extract. However, the concentration at which degranulation started varied widely. Two of the cat allergen extracts (including the one from the Bengal breed), induced PCB degranulation from a dilution of 1:31 250. In contrast, the third extract showed degranulation starting at a dilution of 1: 6250 and the fourth at 1:1250. The cat non-sensitized subject showed no response to all four cat allergen extracts.

Conclusion: This pilot study demonstrated that allergens carried on cat hair varied considerably in their ability to induce basophil degranulation between cats and cat breeds. The work also questions the concept of hypoallergenic cat breed. PCBAT tested with bespoke extracts of cat allergen potentially provides a means to investigate how individual patients react to their own cat.

TP1660 | Clinical significance of detecting specific IgE to cat and dog allergens including major allergen components in pet owners

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Background: The incidence of pet allergies has been increasing. Hence, proper diagnosis of pet allergen sensitization is important. Serologic immunoglobulin E (IgE) measurements of cat and dog allergen extracts are commonly used for identifying pet allergen sensitization. Recently, component-resolved diagnostics-based IgE measurements of allergen components have been used clinically. However, because of cross-reactivity or co-sensitization, the usefulness of IgE measurement assays for allergen extracts or allergen components of pets in pet owners has been questioned.

Method: In total, 188 patients with allergic rhinitis were enrolled in this study. Among them, 139 were pet owners. The patients underwent a skin prick test. Specific IgE (sIgE) in cat (e1) and dog (e5) allergen extracts and those in allergen components (Fel d 1, Can f 1) were measured in the sera of patients. To validate the usefulness of IgE measurements in pet owners, the patients were classified according to pet ownership (non-owners, cat owners, dog owners, and owners of both). The sIgE positivity for each allergen was then compared among groups. Agreements of positivity among skin prick test results, sIgE in allergen extracts, and sIgE in allergen components were also compared. In addition, according to the patients' allergic disease, the sIgE positivity for each allergen was compared.

Results: In the comparison of sIgE positivity for each allergen depending on pet ownership, pet owners showed higher sIgE positivity than non-owners for all allergens. However, among pet owners, sIgE positivity did not show a clinically significant difference. Positivity of sIgE to Fel d 1 was significantly lower in patients with sinusitis (odds ratio: 0.39), and positivity of sIgE to Can f 1 was significantly higher in patients with asthma (odds ratio: 2.5). Results of the skin prick test with cat allergen extracts and sIgE measurements (e1 and Fel d 1) showed more than moderate agreements one another. However, these agreements for dog allergen extracts were poor.

Conclusion: Unlike those of dog allergen extracts, sIgE measurements of cat allergen extracts show consistency with skin prick test results. However, serologic IgE measurements alone are insufficient for the diagnosis of cat and dog sensitization in pet owners. Symptoms and results of skin prick tests should be considered.

TP1661 | Molecular sensitization profile to animal epithelia in an atopic population

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Background: Aim: To evaluate potential cross-reactivity between cat, dog, horse, mouse and cow epithelia in an atopic population through frequency analysis of component resolved diagnosis (CRD) findings.

Method: A bivariate retrospective analysis of ImmunoCAP ISAC® results obtained between 2009-17 was performed using IBM SPSS v23® (Pearson correlation) for animal epithelia (Fel d1,d2,d4; Can f1, f2,f3,f5; Equ c1,c3, Mus m1 and Bos d6).

TABLE 1

Fel d1	Fel d2	Fel d4	Can f1	Can f2	Can f3	Can f5	Equ c1	Equ c3	Mus m1	Bos d6	
1	−0.10	0.14	−0.18	−0.12	−0.05	0.16	−0.04	0.17	0.05	−0.19	Fel d1
	1	0.30	0.02	0.22	0.77	0.03	0.12	0.14	0.12	−0.50	Fel d2
		1	0.12	0.16	0.41	0.10	0.54	0.01	0.69	0.18	Fel d4
			1	0.26	0.11	0.07	0.12	0.07	0.04	−0.01	Can f1
				1	0.32	0.03	0.03	0.18	0.03	0.13	Can f2
					1	0.09	0.18	0.20	0.18	0.66	Can f3
						1	0.10	−0.10	0.01	−0.07	Can f5
							1	−0.07	0.54	−0.05	Equ c1
								1	0.09	0.20	Equ c3
									1	0.18	Mus m1
										1	Bos d6

Results: From a total of 300 samples/300 pts (♀144; 48% ♂156; 52%), mean age 30 ± 15 yrs (4-91), Md 31 yrs, 106 (35%) were sensitized to at least one epithelia: 85 to cat (80%), 52 to dog (49%), 13 to horse (12%), 7 to mouse (7%) and 3 to cow (3%) epithelia. One pt was positive to all epithelia. Regarding CRD evaluation of the 85 cat sensitized pts, 83 (98%) had Fel d1 (0.3-102ISU; mean 12.1 Md 4.8), 5 Fel d2 (6%) and 7 Fel d4 (8%). Eight pts had more than 1 cat component, 2 had all 3. From the 52 pts sensitized to dog 38 (73%) had Can f1 (0.3-70ISU mean 12.4, Md 7.2), 11 Can f2 (21%), 3 Can f3 (6%) and 16 Can f5 (31%). One pt was sensitized to all canine components. Double sensitization to cat and dog components occurred in 36 pts: majority Fel d1 + Can f1 (26; 72% $r = -0.18$). A strong correlation ($r = 0.77$) was observed for Fel d2 + Can f3. Another significant correlation was demonstrated in pts with Fel d4 + Can f3 ($r = 0.41$). These data also showed a positive correlation between cat, horse, mouse and cow lipocalins and albumins. The strength of linear correlations between components is shown in Table 1.

Conclusion: CRD improves the characterization of sensitization to animal epithelia. We evidenced potential cross-reactivity to epithelia between proteins of the same family (lipocalins/albumins) as previously described. A moderate correlation between Fel d4 + Can f3 was interpreted as double sensitization to different protein families.

TP1662 | Allergens in dog extracts and in a dog population: Implication for diagnosis and treatment

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Background: Five to ten percent of the population in affluent countries are allergic to dogs. Seven dog allergens have been attributed to causing allergic symptoms in sensitized individuals. Diagnosis and treatment is based on allergen extracts from naturally derived sources for which information on allergen composition and concentration is lacking. The aim was to quantify six dog allergens (Can f 1-6) in commercial skin prick test (SPT) solutions and to investigate variation in individual dog allergen profiles.

Method: The allergen content of SPT solutions from five vendors and allergen source material from three anatomical sites (hair, dander and epithelia) were analyzed. Fur and saliva samples were collected from a mixed population of 120 dogs. Can f 1-6 were quantified by inhibition ELISA using purified recombinant or natural allergens and polyclonal or monoclonal antibodies. Allergenicity was analyzed by basophil activation test.

Results: Extensive variation in allergen composition was observed in commercial SPT vials resulting in a patient-dependent ability to activate basophils. Extract heterogeneity depended on manufacturer and collection site. Can f 2 and 6 exhibited low levels in fur and SPT solutions, whereas Can f 4, which was the dominating allergen in fur samples did not display similar high proportions in SPT solutions. Can f 3 varied most among SPT solutions, while Can f 5 was significantly higher expressed in fur samples from male dogs compared to females. The allergen profiles in individual dogs varied both within and between breeds.

Conclusion: The great variation of dog allergens in natural extracts raises questions of source, sampling, processing and ultimately of standardization. The need for defined minimum allergen levels for accurate diagnosis and treatment is pressing.

TP1663 | Analysis of sensitization profiles in allergy patients focused on animal allergen molecules

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Background: The increasing presence of animals in households, associated with the presence of their allergens in places where no

animals are present (schools etc.), has contributed to an increase of pet allergy. Frequently observed co-sensitization to more animal diagnostic extracts highlights the importance of molecular diagnosis revealing sensitization to species-specific and cross-reacting allergens. The aim of our study was to assess the usefulness of molecular diagnosis in the description of sensitization profiles in allergy patients focused on animal allergen molecules.

Method: We studied sensitization profiles of allergy patients living in the western part of the Czech Republic. The molecular diagnosis was performed by means of the ImmunoCAP ISAC microarray. 1255 patients sensitized to at least one allergen component were subjected to detailed statistical analysis. We focused on animal-derived allergen molecules presented in ISAC: Fel d 1, Fel d 2, Fel d 4 for cat; Can f 1, Can f 2, Can f 3, Can f 5 for dog; Equ c 1, Equ c 3 for horse; Mus m 1 for mouse and Bos d 6 for cow.

Results: The sensitization rates for cat allergens Fel d 1, Fel d 2 and Fel d 4 were 31.8%, 3.2% and 5.3%. The most frequently was observed monosensitization to Fel d 1, followed by co-sensitization of Fel d 1 with Fel d 4 and Fel d 1 with Fel d 2. Monosensitization to Fel d 4 and Fel d 2 was rare. The sensitization rates for dog allergens Can f 1, Can f 2, Can f 3 and Can f 5 were 13.9%, 4.2%, 2.9% and 16.4%. The most often was monosensitization to Can f 1 and Can f 5, followed by co-sensitization of Can f 1 with Can f 2, Can f 1 with Can f 5, Can f 1 with Can f 3 etc. Monosensitization to Can f 2 and Can f 3 was rare. The sensitization rates to other available animal allergens Equ c 1, Equ c 3, Mus m 1 a Bos d 6 were 6.2%, 1.5%, 4.1% and 1.3%. Detailed analysis of sensitization profiles to lipocalins (Can f 1, Can f 2, Fel d 4, Equ c 1, Mus m 1) and albumins (Can f 3, Fel d 2, Equ c 3, Bos d 6) confirmed high rate of co-sensitization within both groups.

Conclusion: Species-specific cat uteroglobin Fel d1 and dog kallikrein Can f 5 are the most frequently observed animal allergens in our group. Less frequent, but common is sensitization to cross-reactive lipocalins, sensitization to cross-reactive albumins is very low. Commonly observed co-sensitization to more animal diagnostic extracts (cat, dog, horse, mouse) can be mainly explained by sensitization to cross-reactive lipocalins.

TP1664 | Analysis of dust mite allergen components in asthmatic children from Costa Rica and Ecuador: Focus on Der P 23

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Background: Dust mites (DM) are a major source of indoor allergens and IgE to DM are strongly associated with allergic asthma, particularly high-titer IgE that is commonly seen in post-hygiene environments. Der p 1 and 2 are well-characterized components but the relevance of Der p 10 and 23 in asthma are less clear. Der 23 is a recently described DM allergen but investigations to date have been limited to small cohorts and/or microchip assays. Here we investigate IgE to DM components, Der p 1, 2, 10 and 23 in populations of children where DM sensitization is common using high-capacity ImmunoCAP.

Method: Sera from a study in San Jose, Costa Rica (CR) where high titer IgE to DM was strongly associated with asthma were compared with sera from children in Ecuador where predominantly urban post-hygiene environment exists in parallel with predominantly rural pre-hygiene conditions. Sera that were positive for specific-IgE (sIgE) to *D. pteronyssinus* (*Dp*) (cut-off of 0.35 IU/mL) were assayed by ImmunoCAP for sIgE to Der p 1, 2, 10 and 23 (cut-off of 0.35 IU/mL).

Results: Geometric mean IgE titers to *Dp* were 23.9 IU/mL (95% CI 18-32) in CR and 2.8 IU/mL (95% CI 2-4) in Ecuador. Der p 1, 2, 10 and 23 were common in DM-sensitized subjects from CR (69%, 69%, 17% and 64%) and Ecuador (45%, 32%, 19 and 33%). In Ecuador, Der p 1, 2, 10 and 23 components sensitization was 41%, 34%, 11% and 33% for urban and 50%, 28%, 27% and 31% for rural districts. Geometric mean titers of sIgE to *Dp* components were more pronounced among asthmatics in CR and Ecuador, with a rank order: Der p 2 > Der p 1 > Der p 23 > Der p 10.

Conclusion: Der p 23 represents a peritrophin-like protein of DM that is present at markedly lower levels than Der p 1 and Der p 2 in post-hygiene environment but is nonetheless a major target of IgE in DM-sensitized subjects. Here we show a conserved pattern of component sIgE responses in each of these environments where IgE to mite extracts has been associated with asthma, a finding that was also similar in Ghana and a control cohort in the USA. The high frequency of sensitization to these three proteins, which are structurally distinct and are found in different compartments of the mite, provides strong evidence that these three allergens are significant/major allergen of the DM. Further, high-level sensitization to one or more of the three components was very common in sera with sIgE ≥ 3.5 IU/mL to mite extract, i.e. those results that are strongly associated with asthma.

TP1665 | Evaluation of various methods of clinical and laboratory diagnosis for house dust mite (HDM) sensitisation in patients with HDM-triggered allergic rhinoconjuctivitis

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Background: Currently, diagnosis of allergic rhinoconjunctivitis is based on assessment of IgE-mediated response using skin prick test as the gold standard as well as measurement of serum specific IgE. Allergen Exposure Chamber (AEC) allow to generate exposures

which are well controlled, stable and independent from external factors which might affect the results. Patients with allergic rhinoconjuctivitis require detailed diagnosis and accurate interpretation of test for allergen sensitization in the context of their symptoms. The aim of this study was to compare the results of SPT, sIgE and symptom scores in patients with allergic rhinitis sensitised to house dust mite challenged in AEC.

Method: The study included fifty patients with chronic allergic rhinoconjunctivitis. Allergy to house dust mite was confirmed by SPT (modified Pepys method) and measurement of sIgE (immunoenzymatic method - ®Polycheck). Patients were exposed to HDM allergens in AEC. Symptoms were additionally assessed using Combined Symptom and Medication Score (CSMS), Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) and Visual Analog Scale (VAS).

Results: The majority of patients showed positive SPT to D. farinae and D. pteronyssinus (97% and 92% respectively). In 86% of subjects serum sIgE to house dust mites was positive. 88% of patients had positive SPT results for both D.f. and D.p. All patients positive to house dust mite in serum sIgE test showed sIgE against both D.p. and D.f. A very strong positive correlation was found between wheal area in SPT to D.p. and D.f. ($P < 0.0014$, $r = 0.76$), and between SPT to D.f. and the level of sIgE against D.p. ($P < 0.0014$, $r = 0.68$) as well as between the response to either D.f or D. p., measured by SPT and the level of serum sIgE ($P < 0.005$, $r = 0.55$ for D.f., $P < 0.005$, $r = 0.53$ for D.p.). No significant correlation between response in SPT or sIgE levels and symptom scores assessed during AEC exposure was found. A large number of significant correlations between measurements of TNSS and pollen concentration in AEC were observed. Most of the significant correlations between SPT, sIgE and symptom scores (CSMS, RQLQ and VAS) were negative.

Conclusion: SPT and sIgE should not be the only diagnostic tool in patients with allergic rhinoconjunctivitis to house dust mite. AEC test is a better predictor of clinical sensitization to HDM in allergic rhinoconjunctivitis as compared to SPT or serum sIgE. To assess the severity of symptoms, the validated symptom score scales should additionally be used.

TP1667 | Clinical relevance of dermatophagoides pteronyssinus sensitization in patients with rhinitis

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Background: Sensitization to house dust mite only in clinical terms can be difficult to assess if we consider the non-seasonal nature of the symptoms, the co-sensitizations and the possible role of other agents, such as infections and non-specific irritants. Nasal challenge test (NCT), despite the lack of standardization of methods and criteria for positivity, has been defended by several authors to establish the relevance of allergic sensitization. The aim of our study was to evaluate the relevance of sensitization to *Dermatophagoides pteronyssinus* (Dp) in rhinitis.

Method: Twenty-one patients with rhinitis and suspected allergy to house dust mites were enrolled. Skin prick tests (SPT), NCT to Dp (Diater® extracts) and specific IgE assays (IgEs) for Dp, Der p1 and Der p2 (ImmunoCAP®, Thermo Fisher) were performed. Positive criteria were: SPT with papule maximum diameter (pmd) ≥ 3 mm; IgEs ≥ 0.35 kUA/L; NCT with decreased peak nasal inspiratory flow (PNIF) ≥ 40% or 2 criteria of ≥ 5 sneezing, rhinorrhea, decreased PFIN ≥ 20 from basal value. The sensitization of *Lepidoglyphus destructor* was also investigated.

Results: The mean age of the patients was 29.8 years, median 22.0 (11 to 63 years), 11 patients (52.4%) were male.

The NCT to Dp was positive in 11 patients and in all of them the SPT were positive for Dp (5 to 17 mm pmd); 7 showed positive IgE to Der p1 (1.6 to 78.5 kUA/L), 8 positive IgE to Der p2 (2.8 to 126.0 kUA/L) and 10/10 IgE to Dp (0.7 to 276.0kUA/L).

Of the 10 patients who had negative NCT, 8 had SPT positive to Dp (pmd de 3 a 13 mm), 2 had positive IgEs to Der p1 (15.1 a 33.5 kUA/L), 5 had positive IgEs to Der p2 (4.7 a 40.5 kUA/L) and 6 had positive IgEs to Dp (0.6 a 130 kUA/L). From the 17 patients with positive SPT and at least one positive specific IgE, 6 (35.3%) had a negative NCT. The NCT showed a low correlation with the IgEs for Dp and Der p1 - rho 0.49; did not correlate with SPT. Seventeen patients (81%) were sensitized to Lepidoglyphus destructor, 14 with positive NCT.

Conclusion: Our results suggest that SPT and IgE assay are insufficient to assume the clinical relevance of sensitization. NCT should be used for this purpose.

TP1668 | Sensitization to Blomia tropicalis and Ascaris spp. components in recurrent wheezing children living in a tropical city

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Background: *Blomia tropicalis* and *Ascaris* spp. are cross-reactive sources and important sensitization causes in the Tropics. Few studies have assessed the role of purified allergens on wheezing presentation at early age. We sought to determine the diagnostic performance of a panel of *B. tropicalis* and Ascaris allergens and the relationship between sensitization and symptom severity indicators.

Method: Children (0 - 5 years old) attending the emergency room (ER) of the University Hospital Napoleon Franco Pareja (Cartagena de Indias, Colombia) due to recurrent wheezing (3 or more episodes during the last year) were recruited (n = 202). Serum IgE levels to complete extracts and components (*B. tropicalis*: Blo t 2, Blo

t 5, Blo t 12 and Blo t 21 and *Ascaris spp.*: Asc s 1, Asc l 3 and Asc l 13) were determined in a multiplex-ELISA platform. All components were obtained as recombinant molecules in *Escherichia coli*. A questionnaire was applied to the caregiver to obtain information about disease and symptoms severity (severe dyspnea episodes, night awakenings events, ER visits and hospitalizations during the last year).

Results: Mean age was 1.7 ± SD 1 yrs and 59.4% were males. Sensitization to *B. tropicalis* and Ascaris extracts was 47% and 41%, respectively. Rates of allergen sensitization raised with age in a significant trend ($P < 0.05$), except for Asc l 13 that dropped at 3y. Among those sensitized to *B. tropicalis* extract, rates were 35%, 34%, 28% and 23% to Blo t 2, Blo t 5, Blo t 21 and Blo t 12, respectively. The *B. tropicalis* panel had 41% of sensitivity and 91% of specificity to detect cases identified with the extract, being Blo t 2/Blo t 5 enough to identify all positive results. Sensitization to *B. tropicalis* extract in those negative to Blo t 2, Blo t 5, Blo t 12 and Blo t 21 was barely explained by the cross-reactive tropomyosin Asc l 3 (4 out of 49). Among Ascaris extract (+) children, sensitization was 41% to Asc s 1, 38% to Asc l 3 and 30% to Asc l 13, showing this combination 51% of sensitivity and 91% of specificity. The specific IgE response to any of the analyzed allergens was not associated with severity indicators.

Conclusion: Among wheezers from this tropical population, *B. tropicalis* and Ascaris sensitization is common, but not associated with disease severity. Sensitivity of the current panel of molecules to detect *B. tropicalis* and Ascaris sensitization is close to 50%. More allergens should be evaluated to improve component resolved diagnosis performance from these sources.

TP1669 | Mold spores in the home as a risk factor of allergic asthma

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Background: Indoor mold spores may trigger allergic asthma and rhinitis. Growth of mold depends on temperature, humidity, aeration, and acidity of the indoor environment. Elimination of mold is critical for control of asthma and rhinitis.

Method: 150 adult patients from the pulmonology department were examined. Questionnaires evaluating patient living conditions and mycologic inspection of their premises with biomaterial sampling including air sampling and assessment of mold in culture were all done. Mold was assessed by macroscopic description. Medical evaluation of patients included a home objective survey, skin allergy tests with fungal allergens, house dust and pollen allergens, and assessment of specific immunoglobulin E(sIgE) in serum.

Results: From the Questionnaire, 74(49%) gave a history which needed mycologic inspection of their housing ($P < 0.05$). Mycology inspection was obligatory in 39 (26%) patients ($P < 0.05$). In samples taken on their premises having visual signs of mold, domination of one or two fast-growing cultures of Alternaria (19%), Aspergillus(13%), Penicillium(22%) were observed ($P < 0.05$). Among residents of mold infested premises, 176 adults, 44(25%), had significantly high levels of sIg E ME (25-75%) 4.8(3.6-6.0)IU/mL to fungal allergens, while another 23(13%) of patients had threshold level of sIgE 0.69 (0.52-0.86)IU/mL to fungal allergens ($P < 0.05$). Sensitization to fungi was seen in 38% ($P < 0.05$) of residents of apartments with confirmed fungi contamination.

Conclusion: Almost half of the allergic asthma patients of pulmonology department of city hospital need mycologic inspection of housing. More than 30% of adult residents of apartments with confirmed mold develop sensitization to fungi allergens. Mold elimination in housing is a critical component of treatment of these patients.

TP1670 | Allergen-specific IgE to grass molecular components: Analysis on age, sex and area of provenience

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Background: In the last few years allergic diseases of respiratory system are becoming global health problems. Main respiratory allergies include asthma and rhino-conjunctivitis. Respiratory allergy is characterized by an IgE-mediated reaction, in which allergen is recognized by IgE antibodies. In our study we want to test the hypothesis that age, sex and geographical origin may affect IgE production to the grass in a group of Italian allergic patients.

Method: Subjects who underwent laboratory allergological investigations in the IRCCS Foundation San Matteo of Pavia between September 2010 and November 2016 in order to confirm grass allergy were included in this study. The patients were divided in 9 age groups, for sex and for geographical origin (urban area, rural area, agricultural area). We used ISAC methods and we considered: CynD1, PhlP1, PhlP2, PhlP4, PhlP5, PhlP6, PhlP7, PhlP11 and PhlP12 allergens.

Results: 772 patients were included in the study. We observed that sex, age group and geographical origin may affect the results. In particular, the sensitization for PhlP2 and PhlP6 allergens is more common in men and in patients from urban areas, compared to CynD1, PhlP1, PhlP4, PhlP5.

Conclusion: Our study show that sex, age group, and geographical origin may influence the distribution of allergic sensitization to grasses.

TP1671 | Oropharyngeal symptoms to bell pepper in an adult patient with Bet V 1-related allergy

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Case report: Allergy to bell pepper (*Capsicum annuum*) also called sweet pepper (*Solanaceae* family) has been reported as occupational respiratory allergy to its pollen and as food allergy to eating the raw fruit, including anaphylaxis. Known fruit allergen molecules include thaumatin-like protein Cap a 1, profilin Cap a 2, ascorbic acid oxidase Cap a 30 kD, Cap a glucanase, and the Bet v 1-like Cap a 4.

We present a 32-year-old female patient with seasonal *Betulaceae* pollen allergic rhinoconjunctivitis, and convincing history of oral allergy syndrome to apple, carrot and celery, reporting immediate severe oropharyngeal allergy symptoms each time after eating raw sweet bell pepper. Skin prick testing was performed with commercial pollen allergen extracts and celery, while prick-prick testing was done with several Bet v 1-containing plant foods: hazelnut, apple, peach, carrot, and fresh bell pepper from Southern Romania. The *in vitro* allergy diagnosis was performed using multiparameter line blot immunoassays with native extracts and recombinant molecular allergen components. Regarding the Bet v 1-related allergy, the patient presented positive skin prick tests to commercial extracts of birch and hazel pollen (each 6 mm diameter wheal), celery (5 mm wheal), and positive prick-prick tests with fresh bell pepper (7 mm wheal), apple (10 mm wheal), carrot (6 mm wheal), peach and hazelnut (each 4 mm wheal), while serum specific IgE levels were found significantly increased for native pollen extracts of birch (90 kU/L), hazel (72 kU/L) and alder (69 kU/L). Serum specific IgE antibodies were detected against *Rosaceae* fruits, apple (0.43 kU/L), peach (59 kU/L) and hazelnut (21 kU/L), and *against Apiaceae* vegetables, celery (8.5 kU/L) and carrot (2.4 kU/L). Specific IgE profile to recombinant components revealed sensitization to rBet v 1 (76 kU/L), while serum IgE antibodies to profilin (rBet v 2, rPhl p 12) and polcalcin (rBet v 4, rPhl p 7) biomarkers, and to isoflavone reductase rBet v 6, were not detected (<0.35 kU/L). Serum IgE level to cross-reactive carbohydrate determinant was also below detection (<0.35 kU/L).

Betulaceae pollen-related food allergic patients should be questioned about oropharyngeal or other allergy symptoms occurring when eating raw foods from a panel list of potentially Bet v 1-cross-reactive plant foods, not only hazelnuts and apples, but also bell pepper.

Consent to publish: Written informed consent was obtained for presentation and publication.

TP1672 | Prevalence of sensitization to lipid transfer protein (LTP) and profilin in a sample of 221 patients in Santiago, Chile

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Background: Panallergens are extended proteins in the vegetal kingdom with sequences and structures highly conserved, able to induce cross-reactivity between pollens and vegetables. Lipid transfer protein (LTP) and profilin are the most important panallergens in the management of patients with respiratory allergy and food allergy. LTPs are highly stable proteins that can induce systemic symptoms after ingestion while profilins are labile proteins that generate symptoms exclusively in the oral cavity.

Method: The results of airborne and foods allergens prick tests (PT) of 221 patients referred to the Allergy Center of the UC-Christus Health Network, Santiago, Chile, between November 2017 and April 2018, were analyzed. The allergens used included commercial extracts (Leti®, ALK® and Diater®) and extract of LTP and profilin (Bial-Arístegui®).

Results: The average age of the individuals was 20.9 years (6 months to 87 years), 59.3% of whom were women. In the analyzed population, 41.6% only had positive PT to airborne allergens, 3.6% only had positive PT to food allergens and 26.7% had both PT positive. It was found that 3.2% were sensitized to LTP, 7.7% to profilin and only one subject was sensitized to both panallergens (0.4%). All the patients sensitized to profilin presented sensitization to pollen from grasses or weeds and only half of them were sensitized to some kind of food. Of the patients sensitized to LTP, one of them had negative PT to airborne allergens and the rest presented sensitization to the pollen of grasses or weeds, while all of them presented sensitization to foods, peanut and walnut (57%) being the most prevalent.

Conclusion: Sensitization to panallergens affects 10.9% of the studied population. It is noteworthy that the majority of subjects sensitized to profilin and LTP presented sensitization to pollen from grasses or weeds, whereas food sensitization predominated only in subjects sensitized to LTP, suggesting that primary sensitization to LTP would be via the digestive tract and that of profilins via inhalation.

TP1673 | Sensitization to individual pollen-derived profilins in seasonal allergic rhinitis patients from North Eastern Poland

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Background: Profilins share highly conserved amino acid sequences. The clinical significance and the mechanism of sensitization to

profilins remain not clear. In North Eastern Poland birch, grass and mugwort pollen seasons follow each other but do not overlap. The aim of this study was to compare IgE binding to individual profilins derived from birch, timothy grass and mugwort in seasonal allergic rhinitis patients (SAR).

Method: The study was performed on a group of 48 sensitized to profilins SAR patients. All patients were allergic to birch, grass and/or mugwort pollen, as demonstrated by skin testing and elevated level of serum IgE (>0.7 kU/L) to those allergenic sources. Twenty nonallergic, healthy subjects were used as controls (HCs). Sensitization to individual profilins was demonstrated by ELISA method using recombinant (*r*) profilins of mugwort (Art v 4), birch (Bet v 2) and timothy grass (Phl p 12) pollen. In addition profilin (Amb a 8) from ragweed, which is not present in North Eastern Poland, was used. All recombinant profilins were previously well-characterized structurally and immunologically (JBC 2016;291:15447). In addition ELISA inhibition assay was used to indicate the culprit profilin.

Results: All SAR patients were sensitized to at least 2 pollen allergen sources, and 50% were sensitized to all three: birch, timothy grass and mugwort. In HCs no significant IgE reactivity to any of the profilin studied could be demonstrated. Elevated IgE reactivity to each studied profilin was demonstrated in every SAR patient. The greatest intensity of IgE binding to Phl p 12, Art v 4 and Bet v 2 was demonstrated in 26 (58.2%), 18 (37.5%) and 4 (8.3%) of SAR patients respectively. No simple correlation between the proportion of IgE binding to individual profilins and that to corresponding allergen sources could be found. In less than 30% of patients complete inhibition of the IgE binding to Phl p 12, Art v 4 and Bet v 2 could be achieved with any of the studied profilins used as inhibitors.

Conclusion: IgE response to specific epitopes of pollen profilins play a significant role in the overall response to those allergens being different in individual SAR patients.

TP1674 | Importance of anti-CCD sensitization in patients living in Sahel

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Background: Few works have focused on allergic pathologies in the Sahelian zone. Thirty-seven sera from patients with food (on the basis of medical history) and/or respiratory allergies (asthma authenticated by FEV) were collected in Mali. Some of these sera were analysed by a biochip displaying 282 allergens.

Method: Patient sera (mean age 17 years, SR 0.54) were analysed in France. Clinical information was recorded on a standardized form. Commercial extracts were used for skin tests (ST). All sera were tested by an ImmunoCAP ™ panel (Thermo Fisher Scientific) including total IgE, Phadiatop ™, food mixtures (fx1/fx2/fx3/fx5), and ascaris (*A. lumbricoides*) extract (p1). The ALEX biochip (MacroArray Diagnostics GmbH) was used, together with a CCD-blocker reagent, to study the 18 most sensitized patients.

Results: ImmunoCAP tests showed high total IgE levels (mean: 561 kU/L), a high frequency of sensitization against food extracts (22-65% of patients), phadiatop (65%), and ascaris extract (49%). The ALEX analysis, after pre-incubation of the sera with the CCD-blocker, shows that almost all the IgE reactivities of these patients are directed against carbohydrates. In the presence of the CCD-blocker, only weak reactivities remain for venom components (rApi m1, rPol d5, rVes v 5), weeds (rAmb a 4), grass (rPhl p 7), dust mite extracts, crustaceans (shrimp, crab) and mammalian meats (no anti-αgal IgE was present).

Conclusion: The positivity of some ST, as well as the presence of symptoms, may be related to the cross-reactivity of anti-parasite IgE (helminths, plasmodium) with food or respiratory allergens (e.g. mite or crustacean tropomyosins). Our study suggests that asthmatic patients in Mali mainly present with non-allergic, eosinophilic asthma, aggravated or even caused by exposure to mineral dust (carried by Harmattan wind) and traffic pollution. We estimate that specific IgE assays based on glycosylated extracts or components are of little or no use for studying patients living in the Sahel, and can only be interpreted after blocking anti-CCD IgE.

TUESDAY, 4 JUNE 2019
TPS 60
ALLERGY EPIDEMIOLOGY

TP1675 | Secondhand tobacco smoke exposure in early childhood increases the risk of allergic sensitization

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Background: Tobacco smoking is known to be the cause of a number of health problems, and several studies have suggested its association with allergic sensitization and diseases. However, secondhand smoke (SHS) exposure–allergic sensitization and disease relationship is unclear. This study aimed to determine the contribution of SHS exposure in early childhood in the development of allergic sensitization and diseases.

Method: We obtained data from the hospital-based birth cohort study, Tokyo Children's Health, Illness, and Development study. SHS exposure was defined as the presence of smokers in a family living together by using questionnaires at 3 years. Serum-specific immunoglobulin E (IgE) levels were measured using ImmunoCAP ISAC. Allergic sensitization was defined as positive for Der f 1 (a house dust mite allergen), with allergen-specific IgE ≥ 0.3 ISU. Based on the International Study of Asthma and Allergies in Childhood questionnaire, allergic disease outcomes included current wheeze, eczema, and rhinitis at 9 years. The association between SHS exposure and outcomes were analyzed using multiple logistic regression analysis and adjusted by potential confounders including maternal allergy history, maternal age at pregnancy, maternal smoking during pregnancy, mode of delivery, gestational age at delivery, household income, number of previous livebirths, and sex of the child.

Results: Of the 1550 children born into the cohort, 696 attended the 9-year follow-up visits and underwent a blood examination. SHS exposure at 3 years was associated with Der f 1 sensitization at 9 years (adjusted odds ratio [aOR], 1.44; 95% confidence interval [CI], 1.01–2.06). Females had a lower risk of Der f 1 sensitization than males (aOR, 0.56; 95% CI, 0.41–0.76); however, females with SHS exposure had a higher risk compared to males (aOR, 1.90 vs 1.14; interaction aOR, 2.66) than males. There was no statistically significant SHS exposure–allergic disease association.

Conclusion: SHS exposure at 3 years increases the risk of allergic sensitization at 9 years, especially in females.

TP1677 | The effect of mechanical hot dryer for removing pollens allergens

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Background: Environmental control has been recognized as the basic and essential component of treatment for allergic patients. Pollens are the most common outdoor allergens seasonally and may be spread to indoor environments by clothes contaminated during outdoor activity. This study aimed to evaluate the pollen removal efficacy of sanitize course from Hot dryer (Samsung Electronics Co, Suwon, Korea).

Method: Test loads of 100% cottons were 2 kg in dry and 4 kg in wet condition and size of test fabric is 2x5 cm. Birch, Japanese cider, ragweed, and timothy grass pollens were used. After spread pollen, there store for 8 hours at RT and counted pollen as control by Calberla's stain. The fabrics were fixed on test loads and proceeded the dry and wet sanitized course and counted pollen on the fabric to evaluate pollen removal rate on a loads. We measured remaining allergens in extracts from the contaminated fabrics after the dry and wet sanitize course. The concentrations of allergens (Amb a 1, Bet v 1, Crp j 1, and Phl p 1) in each extracted solution were measured by 2-site enzyme linked immunosorbent assay.

Results: Mean removal rate of pollen concentration was 99.9% for birch, 99.95% for Japanese cedar, 99.84% for timothy grass, and 99.91 for ragweed in dry condition and 96.04% for birch, 95.23% for Japanese cedar, 97.59% for timothy grass, and 98.63 for ragweed in wet condition. Mean removal rate of pollen allergens (Amb a 1, Bet v 1, Crp j 1, and Phl p 1) was 99.8% for birch, 99.8% for Japanese cedar, 99.9% for timothy grass, and 99.9% for ragweed.

Conclusion: Sanitize course of dryer removed more than 95% of the pollens outside of the clothes when the load is dry and wet condition.

TP1678 | Prenatal exposure to tobacco is the risk factor for early childhood asthma – polish mother and child cohort study (REPRO_PL)

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Background: The study was supported by the grant from the National Science Center UMO-2017/25/B/NZ5/02338 and UMO-2014/15/B/NZ7/00998

The prevalence of asthma and allergy in pediatric population have increased over the past two decades. Exposure to environmental factors such as second-hand tobacco smoke has been associated with respiratory outcomes.

Objectives: To assess the relation between prenatal exposure to tobacco smoke (ETS) and early childhood asthma at 2 years of age, and asthma in children age 7-9 years. Additionally, association between cotinine concentration in urine of 7-9 year old children and asthma was determined.

Method: The present study was based on data from the Polish Mother and Child Cohort (REPRO_PL) - a multicenter prospective cohort study established in 2007. The current analysis was restricted to 206 mothers and their children from Lodz district. Exposure to tobacco smoking was assessed according to cotinine measurements in mother's saliva during pregnancy and children's urine at the age of 7-9 years (based on Global Adult Tobacco Survey(GATS). Children's asthma was established according to GINA guidelines. The association between cotinine levels and childhood asthma was analyzed using logistic regression. The cotinine levels in saliva and urine were analysed using high-performance liquid chromatography coupled with tandem mass spectrometry/positive electrospray ionisation (LC-MS/MS-ESI+) and the isotope dilution method.

Results: Positive association between cotinine concentration in mother's saliva and childhood asthma at 2 years of age was found (OR(95% CI): 2.24(1.254-4.017), $P = 0.007$. No relationship was observed neither between cotinine concentration in mother's saliva nor in children's urine and asthma at 7-9 years of age.

Conclusion: Our finding support the hypothesis that maternal prenatal exposure to tobacco is the risk factor for early childhood asthma. Notably, we found no interaction between ETS and presence of asthma in later life. Public health efforts are needed to reduce prenatal ETS exposure.

TP1679 | Sensitization different between adults and children in Southern China: A survey based on real-world medical data

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Background: Sensitization is different in adults and children. This study based on large sample side of real-world medical data to analyze the sensitization of adults and children in South China, and to provide evidence for the prevention of allergic diseases in this region.

Method: A retrospective analysis of 39 831 patients who underwent allergen sIgE testing (ImmunoCAP) from January to December 2017 in several centers city from South China (Guangdong, Guangxi, etc.) was performed. The subjects included 22 835 adults and 16 996 children.

Results: In South China, the highest positive rate of allergens was house dust mite (28.1%), following cockroach (24.3%), shrimp (19.2%), crab (15.8%) and egg (9.9%). The positive rate was highest for cockroach allergies in adults (28.2%) and house dust mite allergies in children (29.2%), respectively. The positive rates of egg and milk allergies were higher in children than in adults ($P < 0.05$). The positive rate for cockroach, shrimp and crab allergies in adults was higher than in children ($P < 0.05$). Cockroaches were risk factors for various allergic diseases, and they had a higher positive rate in most parts of South China. Optimal scaling analysis showed that crab, shrimp and cockroach allergen sIgE were closely associated (Cronbach's $\alpha = 0.891$). At the same time, the positive rate for fungal allergies in children increased gradually in summer and fall and reached a maximum (6.2%) in October. In this study, the proportion of prescriptions for allergy testing by doctors due to skin diseases reached 56.9%.

Conclusion: In South China, skin symptoms are more often suspected as allergic reactions and suggest to allergy testing by physicians. This large sample of allergen IgE statistics was collected from South China. Cockroaches are an important allergen and is associated with a variety of allergic diseases in adults. A comprehensive assessment of allergen avoidance is required especially in those with a combination of shrimp, crab, and house dust mite allergies.

TP1680 | The natural course of inhalant allergen sensitization in the elderly: A 6-year longitudinal follow-up of an elderly general population cohort

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Background: Inhalant allergen sensitization has been suggested to decrease with aging. However, the longitudinal change has rarely been investigated in the elderly. Here we examined a 6-year change in the prevalence of allergic sensitization, using a longitudinal follow-up database of a community-based elderly population cohort.

Method: We analyzed the second survey database of the Korean Longitudinal Study on Health and Aging (KLoSHA II; conducted in 2011-2012), and compared with the baseline database (KLoSHA I; in 2005-2006). Atopic sensitization was defined by skin prick tests for 12 common inhalant allergens. Asthma and rhinitis was assessed by structured questionnaires. Baseline parameters were analyzed in relation to the changes in atopic sensitization status.

Results: Among 855 participants in the KLoSHA I study, 369 elderly subjects were followed up in the KLoSHA II survey. The 6-year change in the prevalence of inhalant allergen sensitization was statistically significant ($P = 0.022$; from 18.7% to 13.8%). Among 12 inhalant allergens, Der f showed the most prominent decrease in

the sensitization rate. During the 6-year follow-up period, 42.0% of originally atopic subjects were found to be still sensitized, but 7.3% of previously non-atopic subjects developed de novo sensitization. Age at the KLoSHA I study was the most significant factor associated with de novo sensitization.

Conclusion: This study showed the trends of decrease in the sensitization to inhalant allergens with aging in the general population of the elderly for the first time in Korea. This study also found a small number of newly sensitized elderly people: baseline age was the most significant factor.

TP1681 | Recently changing pattern of sensitization to aeroallergen in Korean children with allergic diseases: Increasing sensitization to pollen and animal dander

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Background: Allergic diseases have been increasing worldwide over the past few decades. Allergic sensitization is a pivotal risk factor for the development of allergic diseases. The purpose of this study was to examine the change in allergic sensitization pattern of aeroallergens over the last 10 years in children with allergic diseases.

Method: We retrospectively reviewed the medical records of 12 848 children under the age of 18 who performed skin prick test (n = 3852) or serum specific IgE test (n = 8996) to evaluate sensitization from 2007 to 2016 in Seoul, Korea.

Results: Sensitization rate of house dust mite (*Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*) was peaked in 2009 (40.5%) and decreased since then (trend $P = 0.011$). Sensitization to animal dander was increasing during 10 years (5.6% to 13.8%; trend $P < 0.001$, respectively), and tree (birch, oak, and alder) and grass (timothy) pollens were also in similar increasing pattern (3.1% to 12%; 1.0% to 5.2%; trend $P < 0.001$, respectively). Weed pollens (ragweed and mugwort) and mold (Alternaria alternata) sensitization rate was lower than other aeroallergens (maximum 5.6% and 5.7%, respectively) but showing also mild increasing pattern during the study period (trend $P = 0.005$, trend $P < 0.001$, respectively).

Conclusion: Over the past 10 years, sensitization pattern of aeroallergen is changing in Korean children with allergic diseases. We have to keep an eye on it to educate the patients for the allergen avoidance and environmental control and to treat effectively.

TP1682 | Exopolysaccharides isolated from lactobacillus rhamnosus LOCK900 modulate immune response in mouse models of airway allergy

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Background: The increasing prevalence of allergic diseases in industrialized countries during recent decades has been correlated with reduced microbial exposure in western population. Therefore, the use of probiotic bacteria and their bacterial cell components for modulation of allergic immune response has been introduced as an interesting concept.

Method: 1) Two-month-old BALB/c mice were two-times sensitized by ovalbumin (OVA) mixed with one of two exopolysaccharides (EPS) isolated from *Lactobacillus rhamnosus* LOCK900. Seven days after the second immunization, mice were sacrificed and OVA-specific antibodies in sera and cytokine production in spleen cell cultures were determined. 2) Two-month old BALB/c female mice were two-times sensitized by intraperitoneal injection of OVA and asthma-like symptoms were induced by intranasal application of four doses of OVA. Two EPS from *L. rhamnosus* LOCK900 were applied intranasally before each ovalbumin challenge. One day after the last challenge, mice were sacrificed and asthma-like symptoms were evaluated by differential cell counting in bronchoalveolar lavage (BAL), histological staining of lung tissue, determination of humoral response in sera and cytokine response in spleen cell cultures and BAL fluid.

Results: 1) Both EPS significantly diminish the sensitization to OVA in experimental mice, as evidenced by reduced levels of OVA-specific IgE and IgG2a in sera and decreased production of IL-4, IL-5 and IL-13 in splenocytes. 2) Intranasal application of EPS from *L. rhamnosus* LOCK900 before OVA-challenge decreased number of eosinophils and neutrophils in BAL and reduced the infiltration of inflammatory cells in lung tissue assessed by histological staining. OVA-specific humoral immune response in sera of treated mice was not affected by EPS administration, whereas the production of OVA-specific cytokines IL-4, IL-5 and IL-13 was downregulated in spleen cell cultures and BAL fluid.

Conclusion: Exopolysaccharides isolated from *L. rhamnosus* LOCK900 were able to modulate immune response in mouse models of asthma. We foresee that intranasal application of defined bacterial molecules may be promising strategy for alleviation of the symptoms of seasonal airway allergies and asthma. (Supported by grants 19-02261S of the Czech Science Foundation, EMBO Installation grant (to Martin Schwarzer), UMO-2012/05/D/NZ7/02494 of the National Science Centre of Poland and PPN/BIL/2018/1/00005/U/00001 of the Polish National Agency for Academic Exchange).

TP1683 | Sensitization pattern and allergy outcome in pregnancy

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Background: It is currently estimated that almost half of the population in industrialized societies is affected by allergy. Allergy in pregnancy is at least as common as in usual population. Additionally the immunological changes in that state, with the increase in activity of Th2 lymphocytes, can cause allergen sensitization even in subjects negative for allergy in pre-conception period. Factors associated with pregnancy and maternal atopy are being reported to relate to the risk of allergy in offspring. The aim of this study was to evaluate the sIgE sensitization to common allergens in pregnancy and its relation to the symptoms and treatment of allergic conditions.

Method: We investigated 155 pregnant women, aged 25-38 years (median 30), living in metropolitan area, without the pregnancy complication, with normal BMI before pregnancy, for sIgE sensitivity for 20 allergens. The environmental factors - tobacco smoke exposure, pets at home and smoking by mother's parents in the past were also taken into account.

Results: In our population 6.7% of women reported asthma, 22% allergic rhinitis, 9.4% atopic dermatitis and 15.4% food allergy. Allergic rhinitis was the morbidity with highest tendency to become more severe in pregnancy (33.3% more severe). Only 11.8% of pregnant women with allergic conditions were taking any medication for asthma or allergy. 47.3% of women were sensitized to at least one allergen at cut-point 0.35ku/L, within this group only 56.5% reported allergic symptoms. The most common food allergens were: apple (5%), cow milk and wheat flour. The most common inhalant allergens were: dust mites (20%), cat and grass pollens. None of pregnant woman was exposed to tobacco smoke at home. Atopic mothers were significantly less prone to have pets than non-atopic. Pregnant women were more frequently atopic if their parents smoked anytime in the past, but this difference was statistically insignificant. In 9.7% atopic mother accompanied father reporting allergic condition.

Conclusion: Asymptomatic sensitization could be common in pregnancy. Allergic conditions are not worsening at that state in majority of cases. Pregnant women tend to avoid anti-allergic medication. There could be an accumulation of known risk factors for unborn child for having allergy later in life such as maternal atopy, lack of pets exposure and atopy in father.

TP1684 | Beta-lactoglobulin (BLG) accumulates in stable dust associated with zinc: Potential implications for the allergy- and asthma-protective effect

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Background: Living on cow farms protects against asthma and allergies, which has been correlated with the immune-modulating effect of stable microbes and their products. In addition, also aerosolized proteins may play a role. Beta-lactoglobulin (BLG) is a prominent protein from milk, which belongs to the lipocalin family. Lipocalins bind a wide variety of ligands, e.g. siderophore/iron complexes, vitamins or metal ions. Our previous studies revealed that in loaded state, the lipocalin BLG prevents induction of a Th2-response *in vitro* from stimulated cells, and prevents allergy *in vivo* in BALB/c mice. We aimed here to assess in the cattle stable the natural presence, source and state of BLG with associated ligands and the ability to modulate immune cells *in vitro*.

Method: Different dust samples from cattle stables in Austria and Germany were collected together with urine samples from resident animals (female and male cattle). Stable dust extracts (SDE) and urines were analyzed immunochemically for BLG. BLG with or without zinc was tested *in vitro* on PBMC of healthy donors.

Results: The concentration of BLG was determined by BLG-specific ELISA to be 1.2-8.6 ng/mg (mean 4 ng/mg) in SDE and 0-7154 ng/mL (mean 135 ng/mL) in bovine urine. In SDS-PAGE, protein bands could be confirmed as monomeric and dimeric BLG by specific anti-BLG antibodies as well as by mass spectrometry (MS). Size exclusion chromatography-inductively coupled plasma MS (SEC-ICP-MS) identified zinc as ligand of BLG in SDE. In preliminary experiments with PBMC from healthy donors, zinc alone or attached to BLG could decrease the proliferation and viability of CD4 + and CD8 + T-cells in a concentration-dependent manner, whereas BLG alone had no such effect.

Conclusion: BLG is a major compound in stable dust, derived from cattle urine. Zinc was found to be attached to BLG in dust and could concentration-dependently suppress T-cell proliferation and viability *in vitro*. We propose that aerosolized BLG and its ligands contribute to the allergy-protective effect of certain cowsheds.

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Conflict of interest: EJJ declares shareholdership in Biomedical Int. R+D GmbH, Vienna, Austria. EJJ and FRW are inventors on patents EP 2894478 A1, US20160334418, WO2015104270A1.

TP1685 | Relationship of the changes in the prevalence of allergic diseases and changes in environmental factors - a cohort study of elementary school

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Background: The prevalence of allergic diseases that lowers the quality of life is steadily increasing, and the change of environmental factors can affect the prevalence of allergic diseases. The purpose of this study was to investigate the changes in the prevalence of allergic diseases and the changes of the environmental factors, and to examine the relationship between these two factors.

Method: In this study, 390 elementary school children from 3 regions that had different characteristics of air quality in Ulsan, Korea were conducted two follow-up surveys (2009-2010, 2013-2014) to investigate the changes in the prevalence of allergic diseases and the changes of environmental factors. The surveys were based on the questionnaire of International society of asthma and allergy of children (ISAAC). We analyzed these data with Chi-square test, McNemar test and Generalized estimating equations.

Results: During the follow-up period, allergic dermatitis decreased, while allergic rhinitis and allergic conjunctivitis tended to increase. In the analysis of causality between environmental factors and allergic diseases, parental smoking and humidifier use were related to allergic rhinitis. Moving or repairs of home was associated with atopic dermatitis. Pesticide use and air pollution were associated with allergic conjunctivitis.

Conclusion: According to the types of allergic diseases, there are differences in the changes of prevalence and related environmental factors. Differentiated strategies for different types of allergic diseases may be more helpful.

TP1686 | Influence of dog keeping on indoor dust microbiota

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Background: Living with furry pets appears to be protective against allergic diseases and airway infections. Dust-samples from homes with dogs are higher in endotoxin as a surrogate marker for gram negative bacterial components than non-dog household samples. The aim of the study was to characterize the association of dog ownership on house dust bacterial and fungal microbiota.

Method: Floor dust samples were collected in a Finnish (LUKAS2, N = 182, living room floor) and a German (LISA, N = 282, bedroom floor) birth cohort study. Dog ownership was asked by questionnaires. The bacterial and fungal composition in the floor dust was characterized by Illumina MiSeq sequencing. The effect of dog ownership on alpha-diversity was analyzed using Mann–Whitney *U*-tests and on the relative abundance of different taxa by ANCOM.

Results: LUKAS2 had 56 (30.8%) dog households and LISA 18 (6.4%). Dog ownership was consistently and positively associated with bacterial richness, i.e. the number of different species (medians in dog households vs non-dog households, 928 vs 805, $P = 0.05$ in LUKAS2 and 907 vs 756, $P = 0.003$ in LISA). The sum of relative abundance of low abundant bacterial genera (mean relative abundance < 1%) were higher (medians: 52% vs 40%, $P < 0.001$ in LUKAS2 and 60% vs 48%, $P = 0.01$ in LISA) in dog households than in non-dog households. No such associations were found with fungi. In LUKAS2 20 and in LISA 28 bacterial genera were associated with having a dog; five of those genera were observed in both cohorts. Only two of these five genera were increased by dog ownership: *Clostridium* and *Megamonas*.

Conclusion: Dog ownership was associated with increased bacterial, but not fungal, diversity in house dust, but had few consistent associations with specific bacterial genera.

TP1687 | Factors associated with development of oral allergy syndrome: A retrospective questionnaire survey from Japanese university students

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Background: To investigate the prevalence and underlying risk of developing oral allergy syndrome (OAS) in Japan, a retrospective cohort study was conducted.

Method: In 2018, a survey was presented to freshman at Osaka University. Data were amassed from 2767 effective responses and assessed by logistic regression analysis.

Results: The lifetime prevalence of OAS was 5.2% of the total. The age of OAS onset peaked bimodally between 0 and 10 years old, with the latter consistent with the peak age of allergic rhinitis onset. There was no significant difference in the age of onset of OAS between males and females. The odds ratio (95% confidence interval) with atopic dermatitis and allergic rhinitis were 6.0 (4.15-8.70) and

6.18 (3.88-9.83), respectively. When subjects had a history of atopic dermatitis exacerbated with food, their odds ratio of developing OAS was 10.8 (5.53-21.26), and environmental factors such as dust, sweat, and skin dryness also showed significant correlation. Patients diagnosed with allergic rhinitis due to birch pollen had an 8.3 (3.74 - 18.53) times higher risk of developing OAS.

Conclusion: Besides allergic rhinitis for birch pollen, atopic dermatitis associated with environmental factors (e.g., diet, dust, and sweat) could be underlying risk factors for the development of OAS.

TP1688 | The relationship between clinical findings of childhood atopical dermatitis and serum vitamin D levels

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Background: Atopic dermatitis is chronic inflammatory disease caused by the complex interaction of genetic, immune and environmental factors and seen especially in infancy and early childhood. In many studies relationship between vitamin D and atopic dermatitis is studied because of the vitamin D's effect on epidermal barrier growth and immunological mechanisms. Purpose of our study is finding relationship a between atopic dermatitis clinical severity, laboratory findings and serum vitamin D levels.

Method: Thirty girls and fifty-four boys, aged between 3 months-5 years included the study. Patient's clinical story, physical examination notes, treatment information, laboratory measurements (serum total IgE levels, blood eosinophil count, radioallergosorbent testing results (RAST) (specific IgE for egg white, cow milk), skin prick test results were evaluated. Patients' atopic dermatitis clinical severity was determined with SCORAD index. Patients' serum vitamin D levels studied in their clinical visits. Serum vitamin D levels were categorized as < 12 ng/mL deficiency, 12-20 ng/mL insufficiency, >20 ng/mL sufficient

Results: Twenty-three percent of patients had high serum total Ig E levels, 32% of patients' RAST levels (specific IgE for cow milk and/or egg white) were higher than 0.35 kIU/L and 23% of patients in this group had positive skin prick tests. Twenty five percent of patients had extrinsic atopic dermatitis, 34.5% of patients had intrinsic atopic dermatitis and 42.8% of all patients had additional atopical disease. Patients' AD severity was categorized considering by SCORAD index and 46.4% of all patients was mild, 40.5% of all were moderate, 13.1% of all were severe. Patients' vitamin D levels determined as deficient in six patient, insufficient in 15 patient, sufficient in 63 patient.

Conclusion: There was no significant difference for SCORAD index, serum total IgE levels, blood eosinophil count, skin prick test results, additional atopical disease between patient groups (categorized for vitamin D levels). There is a need for further studies about relationship between vitamin D levels and atopic dermatitis severity because of the conflicting results of previous studies.

TP1689 | Patch test is helpful in the majority of oral contact allergy patients due to dental materials

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Background: Patch tests with allergens found in dental devices are recommended in diagnosing the causative agents of oral contact allergies; however, the outcome of subsequent restoration of the dental materials is not fully known.

Aim: The aim of the study was to assess the role of dental patch testing in guiding dentists to decide the need of restoration of dental implants in the patients with oral signs and symptoms.

Method: 144 patients with oral signs and symptoms who were referred to our adult allergy clinic between 2013 and 2018 for the diagnosis of oral contact allergies due to dental devices were included in the study. Standard patch tests containing 31 different dental allergens were applied according to the literature. The clinical data of the patients were collected from their clinical records as well as according to a telephone interview performed to learn their current situations whether their complaints have resolved after restoration of dental devices according to the dental patch test results.

Results: The mean age of the patients was 55.9 ± 6.5 years and 82.6% of them were female. In 85 patients, positivity to at least an allergen was observed and the most common allergens detected in the tests were nickel sulfate (n = 43), gold sodium (n = 32), cobalt chloride (n = 17), copper sulphate (n = 15) and palladium salts (n = 14). Most of the patients (71.7%) who had metal incompatibility as a compliant had at least one positivity in the test ($P = 0.018$) and had higher nickel and palladium salts positivity ($P < 0.001$) (Table 1). In 86 patients, dental implants were restorated. After restorations of dental implants in 52 patients who had at least one positivity in the test, improvement of the signs and symptoms was detected in 39 patients ($P = 0.017$).

Conclusion: Patch tests with dental allergens were helpful in three quarters of the patients to decide a restoration of dental materials. Metal incompatibility was an important symptom associated with allergy to dental devices specially to nickel and palladium salts.

TABLE 1 The relationships of the signs and symptoms with tests results regarding most common positive allergens

Signs or symptoms	Potassium dichromate			Cobalt chloride			Gold sodium			Nickel sulfate			Copper Sulfate			Palladium chloride			Sodium tetrahydro-chloro palladate		
	+n (%)	−n (%)	*P*	+n (%)	−n (%)	*P*	+n (%)	−n (%)	*P*	+n (%)	−n (%)	*P*	+n (%)	−n (%)	*P*	+n (%)	−n (%)	*P*	+n (%)	−n (%)	*P*
Metal incompatibility (n = 60)	4 (68.7)	56 (93.3)	NS	8 (13.3)	52 (86.7)	NS	13 (21.7)	47 (78.3)	NS	32 (53.3)	28 (46.7)	<0.001	10 (16.7)	50 (83.3)	NS	14 (23.3)	46 (76.7)	<0.001	16 (26.7)	44 (73.3)	<0.001
Burning in the mouth (n = 77)	9 (11.7)	68 (88.3)	NS	10 (13.0)	67 (87.0)	NS	15 (20.5)	62 (80.5)	NS	27 (35.1)	50 (64.9)	NS	10 (13.0)	67 (87.0)	NS	7 (9.1)	70 (90.9)	NS	6 (7.8)	71 (92.2)	NS
Wound in the mouth (n = 71)	6 (8.5)	65 (91.5)	NS	9 (12.7)	62 (87.3)	NS	13 (18.3)	58 (81.7)	NS	23 (32.4)	48 (67.6)	NS	8 (11.3)	63 (88.7)	NS	3 (4.2)	68 (95.8)	NS	5 (7.0)	66 (93.0)	NS
Pain in the mouth (n = 75)	7 (9.3)	68 (90.7)	NS	9 (12.0)	66 (88.0)	NS	15 (20.0)	60 (80.0)	NS	26 (34.7)	49 (65.3)	NS	8 (10.7)	67 (89.3)	NS	6 (8.0)	69 (92.0)	NS	5 (6.7)	70 (93.3)	NS
Erythema in the mouth (n = 72)	7 (9.7)	65 (90.3)	NS	9 (12.5)	63 (87.5)	NS	15 (20.8)	57 (79.2)	NS	25 (34.7)	47 (65.3)	NS	8 (10.1)	64 (88.9)	NS	6 (8.3)	66 (91.7)	NS	6 (8.3)	66 (91.7)	NS
Dry mouth (n = 52)	3 (5.8)	49 (94.2)	NS	7 (13.5)	45 (86.5)	NS	6 (11.5)	46 (88.5)	0.03	21 (40.4)	31 (59.6)	0.05	6 (11.5)	46 (88.5)	NS	4 (7.7)	48 (92.3)	NS	4 (7.7)	48 (92.3)	NS
Oral lichenoid lesions (n = 42)	4 (9.5)	38 (90.5)	NS	4 (9.5)	38 (90.5)	NS	6 (14.3)	36 (85.7)	NS	13 (31.0)	29 (69.0)	NS	7 (16.7)	35 (83.3)	NS	4 (9.5)	38 (90.5)	NS	3 (7.1)	39 (92.9)	NS
Pruritus (n = 48)	4 (8.3)	44 (91.7)	NS	4 (8.3)	44 (91.7)	NS	14 (29.2)	34 (70.8)	NS	20 (41.7)	28 (58.3)	0.019	8 (16.7)	40 (83.3)	NS	7 (14.6)	41 (85.4)	NS	9 (81.3)	39 (18.8)	0.01

*NS: Non significant.

TP1690 | Genotype associations of atopic march at children

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Background: The atopic march (AM) in pediatrics remains an unresolved problem due to the lack of personalized diagnostic tools for detecting the risk genotypes of the onset and progression of its nosologies: atopic dermatitis (AD), seasonal allergic rhinoconjunctivitis (SARC), perennial allergic rhinitis (PAR) - and, finally, bronchial asthma (BA) as the final step of AM. The updated AM paradigm considers single nucleotide polymorphisms (SNP) of genes involved in AM pathogenesis pathways. Respectively, SNP rs7216389 of sphingolipid biosynthesis regulator 3 gene (*ORMDL3*, chromosome region 17q21.1) is being reported as the one associated with onset and progression of AM and particularly, BA.

Method: We performed the first study in Ukraine of the SNP ORMDL3 rs7216389 gene associations with AD, SARC, PAR, BA at children. We had recruited 119 atopic children from 2 to 17 years into the main group (MG). The control group (CG) consisted of 34 non-atopic children aged from 3 to 17 years old suffering from the disorders of gastro-intestinal tract who had neither allergy clinical manifestations nor positive individual and family allergy history. All the patients were genotyped using rs7216389 allelic discrimination assays for polymerase chain reaction with restriction fragment length polymorphism (PCR-RFLP).We applied Spearman Rank-Order correlation (R) and Fisher exact test two-tailed (FET) values (validated by the *P*-value level (<0.05)); odds ratio (OR) with a 95% confidence interval (CI).

Results: We obtained the statistically significant association of *ORMDL3* rs7216389 T/T variant with MG patients: 33.6% compared to 11.8% in the CG, FET *P*-value = 0.017, R=+0.201 (*P* = 0.013), and the OR = 3.8 (CI 1.24; 11.63). We detected the significant associations between SNP *ORMDL3* rs7216389 T/T variant and 3 AM nosologies. SARC: MG = 40.4% compared to CG = 11.8%, FET *P*-value = 0.004, OR = 5.07 (CI 1.55; 16.61). PAR: MG = 35.4% compared to CG = 11.8%, FET *P*-value = 0.021, OR = 4.11 (CI 1.22;13.90). Finally, we detected the strikingly high association of *ORMDL3* rs7216389 T/T with the incidence of BA: 57.9% in MG compared to 11.8% in CG, FET *P*-value = 0.0009, OR = 10.31 (CI 2.050;42.62).

Conclusion: There is a 3.8 fold positive association of genotype ORMDL 3 rs7216389 T/T with AM nosologies at children. Carriers of the SNP ORMDL3 rs7216389 T/T genotype are of a 5.07, 4.11 and 10.31 fold higher risk respectively for SARC, PAR and BA incidence.

TP1692 | Epidemiology of allergic diseases among schoolchildren in Kuwait: A cross-sectional study

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Background: Allergic diseases including asthma, rhinitis, and eczema are common chronic diseases that affect children and adults. This study aimed to describe the prevalence and determinants of allergic diseases among adolescents in Kuwait.

Method: Schoolchildren aged 11-14 years (n = 3864; 1695 boys and 2169 girls) were enrolled in a cross-sectional study. Parents completed questionnaires regarding their children's early life exposures and clinical history and symptoms of asthma, rhinitis, and eczema. Allergic diseases status was ascertained using previously published clinical criteria. Allergic multimorbidity was defined as the coexistence of allergic diseases in the same individual. Associations between different factors and allergic diseases prevalence were assessed using Poisson regression with robust variance estimation, and adjusted prevalence ratios (aPR) and 95% confidence intervals (CI) were estimated.

Results: The 12-month prevalence estimates of asthma, rhinitis, and eczema were calculated to be 15.7% (600/3829), 28.6% (1040/3643), and 10.2% (388/3791), respectively. The coexistence of "asthma and rhinitis" (3.8%, 141/3738) was the most frequent allergic multimorbidity. Asthma, rhinitis, and eczema coexisted in 1.2% (43/3738) of the study participants. Boys were more likely than girls to have asthma (aPR = 1.88, 95% CI: 1.61-2.20) and rhinitis (aPR = 1.38, 95% CI: 1.18-1.62), whereas eczema affected boys and girls equally (aPR = 0.98, 95% CI: 0.80-1.19). Obesity, household environmental tobacco smoke (ETS) exposure, household cat exposure during infancy, and maternal and paternal history of doctor-diagnosed asthma were associated with increased prevalence of asthma. Rhinitis prevalence was increased in the following subgroups: obese children (compared to those with normal weight), children delivered via cesarean section (compared to those delivered vaginally), those exposed to dogs in infancy, and children with maternal and paternal history of doctor-diagnosed rhinitis. Increased prevalence of eczema was seen among underweight children compared to those with normal weight, children exposed to ETS, and those with maternal and paternal history of doctor-diagnosed eczema. Parental history of allergic disease was associated with allergic multimorbidity in the offspring.

Conclusion: Allergic diseases are prevalent among schoolchildren in Kuwait and parental history of allergy is a strong common determinant.

TP1693 | Level of knowledge about anaphylaxis among students in the final year of medical school

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Background: Anaphylaxis (AA) is considered a serious, potentially fatal disease, with an increase in its incidence, and difficulty in diagnosis and management, particularly by health professionals. The objective of this study is to evaluate the knowledge about diagnosis and treatment of anaphylaxis among students in the final year of medical school.

Method: Cross-sectional study with a self-completed modified questionnaire including 15 items, applied to students in the final year of the Medical school

Results: 75 questionnaires were included, 76% were students of clinical specialties. 56% were female, mean age 24.98 ± 3.09 years. All of them agreed that anaphylaxis can be life threatening reaction. 28% had ever met a patient with anaphylaxis and 17% had ever treated a patient with anaphylaxis. 20% (15/75) answered the questions about the symptoms of anaphylaxis correctly, 90% did not associate gastrointestinal symptoms. Regarding the validated diagnosis of the National Institution of Allergy and Anaphylaxis (NIAID/FAAN), 32% answered correctly and included all three criteria. None of the students answered that reduction of blood pressure is a symptom of anaphylaxis when there is a known allergen. Most of the students (93%) indicated that epinephrine should be administered as a first action if a patient was suspected of anaphylaxis but only 33% agreed that epinephrine might be re-administered in 5 minutes in case of no response. 57% recommended the appropriate route of epinephrine administration, and 44% the appropriate site. 65% did not know the dose of epinephrine for children and adults. 65% agreed to follow up patients for at least 8 hours and 76% agreed to refer the patient to an allergy clinic and 58% have heard about epinephrine auto-injector.

Conclusion: Our answers show better results in relation to other national studies with physicians, but until now, we are diagnosing and managing anaphylaxis inadequately. We should develop educational programme to prevent misdiagnosed cases and deaths from anaphylaxis.

TP1694 | Early introduction of solids into infants' diets may reduce the risk of food allergy development

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Background: This study investigated the cumulative incidence of self-reported food allergy or food intolerance among schoolchildren from two Swedish towns. It also assessed the risk factors associated with food allergy or intolerance.

Method: Questionnaires were used to collect data on food allergy or intolerance in children aged 7-8 years from Mölndal in southwestern Sweden and Kiruna in northern Sweden. Questions were included concerning specific food allergy/intolerance to cows' milk, hens' eggs, fish, peanuts, tree nuts, and cereals, as well as on the onset, cessation, and type of symptoms. Information was also gathered on family allergy history, dietary habits, and certain lifestyle aspects.

Results: Of 1838 questionnaires distributed, 1029 were returned – 717/1354 (53%) from Mölndal and 312/484 (64%) from Kiruna. The cumulative incidence of food allergy or intolerance was 19.6% with a significantly higher cumulative incidence in Kiruna (28.5%) than in Mölndal (15.7%), and solids were introduced at a later age in Kiruna. Introduction of solids into a child's diet after the age of 6 months (adjusted odds ratio 2.0; 95% CI 1.2-3.2) and maternal history of allergic disease (adjusted odds ratio 1.6; 1.1-2.3) were significant risk factors for developing food allergy/intolerance.

Conclusion: There was a substantially higher cumulative incidence of self-reported food allergy/intolerance in the north vs southwest of Sweden. The later introduction of solids in an infant's diet in Kiruna may be one factor explaining the higher prevalence in the northern region.